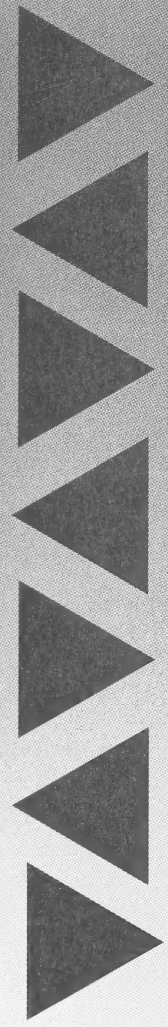
3RD EDITION

GLOSSARY OF HIV/AIDS-RELATED TERMS



HIV/AIDS TREATMENT INFORMATION SERVICE

1-800-HIV-0440

JUNE 1999

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INTRODUCTION

The third edition of the *Glossary of HIV/AIDS-Related Terms* has been updated to include new words commonly used to describe HIV, its pathogenesis, its associated treatments, and the medical management of related conditions. Recent advances in the field of immunology have increased the understanding of how the virus works. New methods for measuring the virus in the blood have changed the way patients are managed, and the use of combination therapies has provided more treatment options than ever before. Definitions for new terms have been added and updates to some of the existing terms are also included in this third edition.

The six U.S. Department of Health and Human Services (DHHS) agencies that cosponsor the HIV/AIDS Treatment Information Service (ATIS) were instrumental in reviewing and supporting this effort. ATIS is a free telephone reference service for health care providers and persons with HIV infection. It provides the latest information about federally approved treatment guidelines. With the frequent updates to these guidelines being released through ATIS, it is essential for care providers and persons living with HIV / AIDS to know how to access this service.

The numbers to use in order to contact the HIV/AIDS Treatment Information Service and other access routes to this service are:

Toll-Free Number: 1–800–448–0440 *Spanish available*
TTY: 1–888–430–3739
Fax Number: 1–800–519–6616
E-mail: atis@hivatis.org
Internet Address: http://www.hivatis.org

Hours: Monday–Friday, 9 a.m. to 7 p.m., Eastern Time

The DHHS agencies that sponsor the HIV/AIDS Treatment Information Service and this glossary are:

Centers for Disease Control and Prevention (CDC)
Health Care Financing Administration (HCFA)
Health Resources and Services Administration (HRSA)
Indian Health Service (IHS)
National Institutes of Health (NIH)
Substance Abuse and Mental Health Services Administration (SAMHSA)

The following is a list of other federal resources that can be contacted for additional information about HIV/AIDS:

AIDS CLINICAL TRIALS INFORMATION SERVICE (ACTIS)

Toll-Free Number: 1–800–874–2572 *Spanish available*
TTY: 1–888–430–3739
Fax Number: 1–800–519–6616
E-mail: actis@actis.org
Internet Address: http://www.actis.org

Hours: Monday–Friday, 9 a.m. to 7 p.m., Eastern Time
Service: Provides information on clinical trials that evaluate experimental drugs and other therapies for adults and children at all stages of HIV infection.

CENTERS FOR DISEASE CONTROL AND PREVENTION, NATIONAL PREVENTION INFORMATION NETWORK (CDCNPIN)

Toll-Free Number: 1–800–458–5231 *Spanish available*
TTY: 1–800–243–7012
Fax Number: 1–800–282–7681
E-mail: info@cdcnac.org
Internet Address: http://www.cdcnpin.org

Hours: Monday–Friday, 9 a.m. to 7 p.m., Eastern Time
Service: The CDC National Prevention Information Network (NPIN) is a national reference, referral and distribution service for information on HIV/AIDS, STDs, and TB. All of the NPIN services are designed to facilitate sharing of information and resources among people working in HIV, STD, and TB prevention, treatment and support services. NPIN staff serves a diverse network of people who work in international, national, state, and local settings.

CENTERS FOR DISEASE CONTROL AND PREVENTION NATIONAL AIDS HOTLINE (CDC NAH)

Toll-Free Number: 1–800–342–AIDS
Spanish: 1–800–344–SIDA
TTY: 1–800–243–7889

Hours: 24 hours
Service: The CDC National AIDS Hotline provides education and information on HIV/AIDS issues, including transmission, prevention, and testing, and referrals to persons with HIV, their families and friends, the general public, and health care professionals.

HRSA NATIONAL CLINICIAN'S POST-EXPOSURE PROPHYLAXIS HOTLINE

(For health care providers only)

- Toll-Free Number: 1–888–HIV–4911

Hours: Monday–Friday, 7:30 a.m. to 5 p.m., Pacific Time.
Emergency calls 24 hrs/day, 7 days/week
Service: This service is for clinicians providing care for those who have sustained occupational exposures to blood and other potentially infectious body fluids.

HRSA NATIONAL HIV TELEPHONE CONSULTATION SERVICE (WARMLINE)

(For health care providers only)

Toll-Free Number: 1–800–933–3413
Internet Address: http://itsa.ucsf.edu/~libbys/warmline.html

Hours: Monday–Friday, 7:30 a.m. to 5 p.m., Pacific Time.
Voice mail available 24 hrs/day
Service: Health professionals from the University of California at San Francisco (UCSF) offer physicians and other health care providers timely HIV clinical information and case consultation across the broad range of clinical HIV/AIDS problems. Collaboration with the UCSF School of Pharmacy, Division of Clinical Pharmacy, provides special expertise in drug usage.

HEALTH SERVICES/TECHNOLOGY ASSESSMENT TEXT (HSTAT) DATABASE, NATIONAL LIBRARY OF MEDICINE (NLM)

Toll-Free Number: 1–800–272–4787
(Menu Options, select #1, 6, 3, or 2)
Other Number: 1–301–496–0176
Fax Number: 1–301–402–3193
E-mail: nichsr@nlm.nih.gov
Internet Address: http://text.nlm.nih.gov

Service: HSTAT is a free, electronic resource that provides access to the full-text of documents useful in health care decision making. It includes: clinical practice guidelines, quick-reference guides for clinicians, consumer brochures, and evidence reports sponsored by the Agency for Health Care Policy and Research (AHCPR); AHCPR technology assessment reports; National Institutes of Health (NIH) consensus development conference and technology assessment reports; NIH Warren G. Magnuson Clinical Center research protocols; and selected Morbidity and Mortality Weekly Reports (MMWRs). NLM provides access to HSTAT through a number of different methods: a full-text retrieval system through GRATEFUL MED, the NLM gopher, through telnet and ftp (file transfer protocol), and through the Internet.

NATIONAL CLEARINGHOUSE FOR ALCOHOL AND DRUG INFORMATION (NCADI)

Toll-Free Number: 1–800–729–6686
(Menu options, select 5 to talk to reference specialist)
TTY: 1–800–487–4889
Fax Number: 1–301–468–6433
Internet Address: http://www.health.org

Hours: Monday–Friday, 8 a.m. to 7 p.m., Eastern Time
Voice mail available 24 hrs/day
Service: NCADI provides information related to alcohol, tobacco, and other drug issues; prevention; research; treatment; and government funding.

NATIONAL CENTER FOR COMPLIMENTARY AND ALTERNATIVE MEDICINE (NCCAM) CLEARINGHOUSE

Toll-Free Number: 1–888–644–6226
TTY: 1–888–644–6226
Fax Number: 301–495–4957
E-mail: nccam-info@altmed.od.nih.gov
Internet Address: http://altmed.od.nih.gov

Hours: Monday–Friday, 8:30 a.m. to 5 p.m., Eastern Time
Services: The National Institutes of Health (NIH) National Center for Complementary and Alternative Medicine (NCCAM) conducts and supports basic and applied research and disseminates information on complementary and alternative medicine to practitioners and the public. **NCCAM does not serve as a referral agency for various alternative medical treatments of individual practitioners.**

OFFICE OF MINORITY HEALTH RESOURCE CENTER (OMHRC)

Toll-Free Number: 1–800–444–6472
TTY: 1–301–589–0951
Fax Number: 1–301–589–0884
E-mail: Imosby@omhrc.gov
Internet Address: http://www.omhrc.gov

Hours: Monday–Friday, 9 a.m. to 5 p.m., Eastern Time
Voice mail available 24 hrs/day

Service: OMHRC serves as a national resource and referral service on minority health issues. The center disseminates free information on a variety of health topics, including HIV/AIDS, cancer, heart disease, substance abuse, diabetes, infant mortality, and violence.

HIV/AIDS GLOSSARY

ABACAVIR: An FDA approved (12/18/98) nucleoside reverse transcriptase inhibitor (see) for use in combination with appropriate antiretroviral agents (see) for the treatment of HIV infection. Also called Ziagen.

ACQUIRED IMMUNITY: See Passive Immunity.

ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS): The most severe manifestation of infection with the Human Immunodeficiency Virus (HIV). The Centers for Disease Control and Prevention (CDC) (see) lists numerous opportunistic infections and neoplasms (cancers) that, in the presence of HIV infection, constitute an AIDS diagnosis. There are also instances of presumptive diagnoses when a person's HIV status is unknown or not sought. This was especially true before 1985 when there was no HIV-antibody test. In 1993, CDC expanded the criteria for an AIDS diagnosis to include CD4+ (see) T-cell count at or below 200 cells per microliter in the presence of HIV infection. In persons (age 5 and older) with normally functioning immune systems, CD4+ T-cell counts usually range from 500–1,500 cells per microliter. Persons living with AIDS often have infections of the lungs, brain, eyes, and other organs, and frequently suffer debilitating weight loss, diarrhea (see), and a type of cancer called Kaposi's Sarcoma (see). See HIV Disease; Opportunistic Infection; AIDS Wasting Syndrome.

ACTG: See Adult AIDS Clinical Trials Group.

ACTIS: See AIDS Clinical Trials Information Service.

ACTIVE IMMUNITY: Resistance resulting from previous exposure to an infectious agent or antigen (see) may be active and specific, as a result of naturally acquired infection or intentional vaccination (artificial active immunity), or it may be passive immunity (see).

ACUPUNCTURE: A Chinese medical treatment involving the insertion of very fine sterile needles into the body at specific points according to a mapping of "energy pathways." Historically, acupuncture is one component of an overall program of Chinese medicine that includes theory, practice, diagnosis, physiology, and the use of herbal preparations. Acupuncture is used to control pain and to treat other conditions such as allergies or addiction withdrawal. See Alternative Medicine.

ACUTE HIV INFECTION: The 4- to 7-week period of rapid viral replication immediately following exposure. The number of virions (see) produced during primary infection is similar to that produced during several subsequent years of established, asymptomatic infection. An estimated 30 to 60 percent of individuals with primary HIV (see) infection develop an acute syndrome characterized by fever, malaise, lymphadenopathy, pharyngitis, headache, myalgia, and sometimes rash. Following primary infection, seroconversion (see) and a broad HIV–1 specific immune response occur, usually within 30 to 50 days. It was previously thought that HIV was relatively dormant during this phase. However, it is now known that during the time of primary infection, high levels of plasma HIV RNA can be documented.

ACYCLOVIR: (Acycloguanosine.) A nucleoside analog (see) antiviral drug used to treat the symptoms of herpes simplex virus (see) infection, herpes zoster (shingles; see), and sometimes acute varicella zoster virus (chicken pox). Also known as Zovirax.

ADAP: See AIDS Drugs Assistance Programs.

ADENOPATHY: Any disease involving or causing enlargement of glandular tissues, especially one involving the lymph nodes.

ADJUVANT: An ingredient—as in a prescription or solution—that facilitates or modifies the action of the principal ingredient. May be used in HIV therapies or for HIV vaccines.

ADMINISTRATION: (Route of Administration.) How a drug or therapy is introduced into the body. *Systemic administration* means that the drug goes throughout the body (usually carried in the bloodstream), and includes oral (by mouth), intravenous (injection into the vein, IV), intramuscular (injection into a muscle, IM), intrathecal (into the spinal canal), subcutaneous (beneath the skin, SQ), and rectal administrations. *Local administration* means that the drug is applied or introduced into the specific area affected by the disease, such as application directly onto the affected skin surface (topical administration). The effects of most therapies depend upon the ability of the drug to reach the affected area, thus the route of administration and consequent distribution of a drug in the body are important determinants of its effectiveness.

ADULT AIDS CLINICAL TRIALS GROUP (AACTG): The largest HIV clinical trials organization in the world plays a major role in setting standards of care for HIV infection and opportunistic diseases related to HIV/AIDS in the United States and the developed world. The AACTG has been pivotal in providing the data necessary for the approval of therapeutic agents, as well as the treatment and prevention strategies, for many opportunistic infections and malignancies. The AACTG is composed of, and directed by, leading clinical scientists in HIV/AIDS therapeutic research and funded through the National Institute of Allergy and Infectious Diseases (see). **Internet address: http://aactg.s-3.com/.**

ADVERSE REACTION: (Adverse Event.) An unwanted effect detected in clinical trial in participants. The term is used whether or not the effect can be attributed to the intervention under study. See Side Effects.

AEROSOLIZED: A form of administration in which a drug, such as pentamidine, is turned into a fine spray or mist by a nebulizer and inhaled.

AETC: See AIDS Education and Training Centers.

AFFECTED COMMUNITY: Persons living with HIV and AIDS, and other related individuals including their families, friends, and advocates whose lives are directly influenced by HIV infection and its physical, psychological, and sociological ramifications.

AGAMMAGLOBULINEMIA: A nearly total absence of immunoglobulins. See Antibodies.

AGENCY FOR HEALTH CARE POLICY AND RESEARCH (AHCPR): An agency of the U.S. Department of Health and Human Services (see) supporting activities to enhance health care services and improve access to them. **Internet address: http://www.ahcpr.gov**

AGENERASE: See Amprenavir.

AHCPR: See Agency for Health Care Policy and Research.

AIDS: See Acquired Immunodeficiency Syndrome.

AIDS CLINICAL TRIALS INFORMATION SERVICE (ACTIS): Provides quick and easy access to information on federally and privately funded clinical trials that evaluate experimental drugs and other therapies for adults and children at all stages of HIV infection. ACTIS is sponsored by the Food and Drug Administration, the National Institute of Allergy and Infectious Diseases, the Centers for Disease Control and Prevention, and the National Library of Medicine (see entries for these organizations). **Internet address: http://www.actis.org/.**

AIDS DEMENTIA COMPLEX (ADC): A degenerative neurological condition attributed to HIV infection, characterized by a group of clinical presentations including loss of coordination, mood swings, loss of inhibitions, and widespread cognitive dysfunctions. It is the most common central nervous system complication of HIV infection. Characteristically, it manifests itself after the patient develops major opportunistic infections or AIDS-related cancers. However, patients can also have this syndrome before these major systemic complications occur. The cause of ADC has not been determined exactly, but it may

result from HIV infection of cells or inflammatory reactions to such infections.

AIDSDRUGS: An online database service of the National Library of Medicine (see), with information about drugs undergoing testing against AIDS, AIDS-related complex, and related opportunistic diseases. **Internet address: http://igm.nlm.nih.gov/.**

AIDS DRUGS ASSISTANCE PROGRAMS (ADAP): State-based programs funded in part by Title II of the Ryan White CARE Act (see) that provide therapeutics (including devices necessary to administer pharmaceuticals) to treat HIV disease or prevent the serious deterioration of health, including treatment of opportunistic infections. ADAP formularies and eligibility criteria are determined state-by-state with a focus on serving low-income individuals.

AIDS EDUCATION AND TRAINING CENTERS (AETC): The Health Resources and Services Administration (HRSA, see) supports the National AIDS Education and Training Centers (AETCs) Program. This is a network of 15 regional centers that conduct targeted, multidisciplinary HIV education and training programs for health care providers. The mission of these centers is to increase the number of health care providers who are effectively educated and motivated to counsel, diagnose, treat, and manage individuals with HIV infection and to assist in the prevention of high risk behaviors which may lead to infection. Internet address: **http://www.service.emory.edu/SEATEC/AETCdir.html.**

AIDSLINE: An online database service of the National Library of Medicine (see), with citations and abstracts covering the published scientific and medical literature on AIDS and related topics. **Internet address: http://igm.nlm.nih.gov/.**

AIDS-RELATED CANCERS: Several cancers are more common or more aggressive in persons living with HIV. These malignancies include certain types of immune system cancers known as lymphomas (see), Kaposi's Sarcoma (see), and anogenital cancers that primarily

affect the anus and the cervix. HIV, or the immune suppression it induces, appears to play a role in the development of these cancers.

AIDS-RELATED COMPLEX (ARC): 1. A term that has been used by some clinicians to describe a variety of symptoms and signs found in some persons living with HIV. These may include recurrent fevers, unexplained weight loss, swollen lymph nodes, diarrhea, herpes (see), hairy leukoplakia (see), and/or fungus infection of the mouth and throat. Also more accurately described as symptomatic HIV infection. 2. Symptoms that appear to be related to infection by HIV. They include an unexplained, chronic deficiency of white blood cells (leukopenia) or a poorly functioning lymphatic system with swelling of the lymph nodes (lymphadenopathy; see) lasting for more than 3 months without the opportunistic infections required for a diagnosis of AIDS. See AIDS Wasting Syndrome.

AIDS RESEARCH ADVISORY COMMITTEE (ARAC): A board that advises and makes recommendations to the Director, National Institute of Allergy and Infectious Diseases, on all aspects of HIV-related research, vaccine development, pathogenesis, and epidemiology.

AIDS SERVICE ORGANIZATION (ASO): A health association, support agency, or other service actively involved in the prevention and treatment of AIDS.

AIDSTRIALS: An online database service of the National Library of Medicine, with information about clinical trials of agents (e.g., drugs) under evaluation against HIV infection, AIDS, and related opportunistic diseases. **Internet address: http://igm.nlm.nih.gov/.**

AIDS WASTING SYNDROME: Involves involuntary weight loss of 10 percent of baseline body weight plus either chronic diarrhea (two loose stools per day for more than 30 days) or chronic weakness and documented fever (for 30 days or more, intermittent or constant) in the absence of a concurrent illness or condition other than HIV infection that would explain the findings.

ALKALINE PHOSPHATASE: An enzyme normally present in certain cells within the liver, bone, kidney, intestine, and placenta. When the cells are destroyed in those tissues, more of the enzyme leaks into the blood, and levels rise in proportion to the severity of the condition. Measurement of this enzyme is used as an indication of the health of the liver.

ALOPECIA: Loss of hair that frequently occurs in patients undergoing chemotherapy for cancer or suffering from other diseases, such as AIDS, where cell-killing, or cytotoxic, drugs are used.

ALPHA INTERFERON: A protein—one of three major classes of interferons (see)—that the body produces in response to infections. In persons who are HIV positive, elevated interferon levels are regarded as an indication of disease progression. Genetically engineered alpha interferon has been approved by the FDA as a treatment for Kaposi's Sarcoma (see). See Interferon.

ALTERNATIVE MEDICINE: A broad category of treatment systems (e.g., chiropractic, herbal medicine, acupuncture, homeopathy, naturopathy, and spiritual devotions) or culturally based healing traditions such as Chinese, Ayurvedic, and Christian Science. Alternative medicines share the common characteristic of nonacceptance by the biomedical (i.e., mainstream Western) establishment. Alternative medicine is also referred to as "complementary medicine" (see). The designation "alternative medicine" is not equivalent to holistic medicine (see), a narrower term. For more information contact the National Center for Complementary and Alternative Medicine Clearinghouse (NCCAM) online. **Internet address: http://altmed.od.nih.gov/.**

ALUM: Potassium aluminum sulfate, or ammonium aluminum sulfate, used especially as an emetic (i.e., an agent that induces vomiting), an astringent (i.e., a substance that contracts tissues), and a styptic (i.e., a substance that tends to check bleeding by contracting the tissues or blood vessels).

ALVEOLAR: Pertaining to the alveoli sac, the site of gas exchange in the lungs.

AMEBIASIS: An inflammation of the intestines caused by infestation with Entameba histolytica (a type of ameba) and characterized by frequent, loose stools flecked with blood and mucus.

AMINO ACIDS: Any of a class of nitrogen-containing acids. Some 22 amino acids are commonly found in animals and humans. Chains of amino acids synthesized by living systems are called polypeptides (up to about 50 amino acids) and proteins (more than 50 amino acids). See Peptide; Proteins.

AMPRENAVIR: An FDA approved (04/15/99) protease inhibitor (see) for use in combination with other antiretroviral agents (see) for the treatment of HIV-1 infection in adults and children. Also called Agenerase.

ANALOG: In chemistry, a compound with a structure similar to that of another compound but differing from it in respect to certain components or structural makeup, which may have a similar or opposite action metabolically.

ANAMNESTIC RESPONSE: The heightened immunologic reaction elicited by a second or subsequent exposure to a particular antigen such as a pathogenic microorganism (e.g., bacterium, fungus) or antigen (see).

ANAPHYLACTIC SHOCK: A life-threatening allergic reaction characterized by a swelling of body tissues (including the throat) and a sudden decline in blood pressure.

ANEMIA: A lower than normal number of red blood cells.

ANERGY: 1. The loss or weakening of the body's immunity to an irritating agent, or antigen (see). Anergy can be thought of as the opposite of allergy, which is an overreaction to a substance. The strength of the body's immune response is often quantitatively measured by means

of a skin test where a solution containing an antigen known to cause a response, such as mumps or candida, is injected immediately under the skin. Patients may be so immunologically suppressed that they are unable to produce cutaneous (skin) delayed-type hypersensitivity reaction (DTH). Such patients will usually not test positive for tuberculosis (see) on a tuberculin skin test (or Mantoux test). The lack of a reaction to these common antigens indicates anergy. 2. Researchers in cell culture have shown that CD4+T cells (see) can be turned off by a signal from HIV that leaves them unable to respond to further immune system stimulation.

ANGIOGENESIS: The process of forming new blood vessels. Angiogenesis is essential for the growth of tumors, especially Kaposi's Sarcoma (see).

ANGIOMATOSIS: A condition characterized by the formation of a tumor that is composed chiefly of blood or lymphatic vessels. (See also Kaposi's Sarcoma).

ANOREXIA: The lack or loss of appetite that leads to significant decline in weight.

ANTIBIOTIC: A substance, especially one similar to those produced by certain fungi, that kills or inhibits the growth of microorganisms such as bacteria or fungi. Some antibiotics are used to treat infectious diseases.

ANTIBODIES: Molecules in the blood or secretory fluids that tag, destroy, or neutralize bacteria, viruses, or other harmful toxins (antigens; see). They are members of a class of proteins known as immunoglobulins, which are produced and secreted by B lymphocytes (see) in response to stimulation by antigens (see). An antibody is specific to an antigen.

ANTIBODY-DEPENDENT CELL-MEDIATED CYTOTOXICITY (ADCC): An immune response in which antibodies (see) bind to target cells, identifying them for attack by the immune system.

ANTIBODY-MEDIATED IMMUNITY: Also called humoral immunity. Immunity that results from the activity of antibodies (see) in blood and lymphoid tissue (see lymphoid organs).

ANTIFOLATE: An agent that inhibits intracellular (i.e., inside cells) production of folinic acid (see).

ANTIFUNGAL: A substance that kills or inhibits the growth of a fungus (see).

ANTIGEN: Any substance that antagonizes or stimulates the immune system to produce antibodies (see) (i.e., proteins that fight antigens). Antigens are often foreign substances such as bacteria or viruses that invade the body.

ANTIGEN PRESENTATION: The event of providing fragments of foreign proteins including viruses and bacteria to the helper T cells (see). The presentation occurs through the display of the fragments of foreign proteins on the surface of the antigen presenting cells (APC) (see).

ANTIGEN-PRESENTING CELL (APC): The cell type that collects foreign material (antigen, see) and digests it into pieces that can be recognized by the immune system. The APC presents the antigen to the helper T cells (see), the CD4+ T cells; this results in the initiation of expansion of an immune response targeted against the foreign material. APCs are B cells, macrophages, or dendritic cells (see entries for these terms).

ANTIIDIOTYPE: An antibody that recognizes and binds to another antibody (idiotype).

ANTINEOPLASTIC: Inhibiting or preventing the proliferation of tumor cells.

ANTIPROTOZOAL: A substance that kills or inhibits the multiplication of single-celled microorganisms called protozoa (see).

ANTIRETROVIRAL AGENTS: Substances used against retroviruses (see) such as HIV.

ANTISENSE DRUGS: An antisense, nucleic acid-related compound is the mirror image of the genetic sequence that it is supposed to inactivate. It is a synthetic segment of DNA (see) or RNA (see) that locks onto a strand of natural DNA or RNA with a complementary sequence of nucleotides (see). By binding to either the target DNA or RNA, the antisense drug prohibits the normal functioning and expression of the gene. This prevents the building of new virus particles or the infection of new host cells. The antisense drug fomivirsen has been approved by FDA for the treatment of CMV retinitis (see), a viral infection that often leads to blindness in patients with AIDS.

ANTITOXINS: Antibodies (see) that recognize and inactivate toxins produced by certain bacteria, plants, or animals.

ANTIVIRAL: A substance or process that destroys a virus or suppresses its replication (i.e., reproduction).

APHASIA: Loss of ability to speak or understand speech.

APHTHOUS ULCER: A painful oral or esophageal sore of unknown cause that has a deep eroded base. Aphthous ulcers are common in persons living with HIV and are treated with corticosteroids. Thalidomide—a drug used in Europe as a sedative before it was discovered that it caused birth defects—is an experimental, alternate therapy.

APOPTOSIS: "Cellular suicide," also known as programmed cell death. HIV may induce apoptosis in both infected and uninfected immune system cells. Normally when CD4+ T cells (see) mature in the thymus gland (see), a small proportion of these cells are unable to distinguish self from nonself. Because these cells would otherwise attack the body's own tissues, they receive a biochemical signal from other cells that results in apoptosis. See Tumor Necrosis Factor.

APPROVED DRUGS: In the U.S., the Food and Drug Administration (FDA) (see) must approve a substance as a drug before it can be marketed. The approval process involves several steps including preclinical laboratory and animal studies, clinical trials for safety and efficacy, filing of a New Drug Application (see) by the manufacturer of the drug, FDA review of the application, and FDA approval/rejection of application.

ARC: See AIDS-Related Complex.

ARM: One group of participants in a comparative clinical trial, all of whom receive the same treatment. The other arm(s) receive(s) a different treatment regimen.

ARTHRALGIA: A pain in a joint.

ASO: See AIDS Service Organization.

ASPERGILLOSIS: A fungal infection—resulting from the fungus *Aspergillus*—of the lungs that can spread through the blood to other organs. Symptoms include fever, chills, difficulty in breathing, and coughing up blood. If the infection reaches the brain, it may cause dementia (see). Amphotericin B is a recommended treatment. Itraconazole may be considered for less serious disease or for those who cannot tolerate amphotericin B.

ASSEMBLY AND BUDDING: Names for a portion of the processes by which new HIV is formed in infected host cells. Viral core proteins, enzymes (see), and RNA (ribonucleic acid; see) gather just inside the cell's membrane, while the viral envelope proteins aggregate within the membrane. An immature viral particle is formed and then pinches off from the cell, acquiring an envelope and the cellular and HIV proteins from the cell membrane. The immature viral particle then undergoes processing by an HIV enzyme called protease to become an infectious virus.

ASYMPTOMATIC: Without symptoms. Usually used in the HIV/AIDS literature to describe a person who has a positive reaction to one of

several tests for HIV antibodies but who shows no clinical symptoms of the disease.

ATAXIA: Lack of muscular coordination.

ATTENUATED: Weakened or decreased. For example, an attenuated virus can no longer produce disease but might be used to produce a vaccine.

AUTOANTIBODY: 1. An antibody (see) that is active against some of the tissues of the organism that produced it. 2. An antibody directed against the body's own tissue.

AUTOIMMUNIZATION: The induction in an individual of an immune response (see) to its own cells (tissue).

AUTOINOCULATION: Inoculation of a microorganism obtained by contact with a lesion on one's own body, producing a secondary infection.

AUTOLOGOUS: Pertaining to the same organism or one of its parts; originating within an organism itself. For instance, donating your own blood for your future surgery is known as an autologous transfusion.

AZT: See Zidovudine.

B

BACTERICIDAL (BACTERIOCIDAL): Capable of killing bacteria.

BACTERIOSTATIC: Capable of inhibiting reproduction of bacteria.

BACTERIUM: A microscopic organism composed of a single cell. Many bacteria can cause disease in humans.

BACTRIM: See TMP/SMX.

BACULOVIRUS: A virus of insects used in the production of some HIV vaccines. See Vaccine.

BASELINE: 1. Information gathered at the beginning of a study from which variations found in the study are measured. 2. A known value or quantity with which an unknown is compared when measured or assessed. 3. The initial time point in a clinical trial, just before a volunteer starts to receive the experimental treatment undergoing testing. At this reference point, measurable values such as CD4 count are recorded. Safety and efficacy of a drug are often determined by monitoring changes from the baseline values.

BASOPHIL: A type of white blood cell, also called a granular leukocyte, filled with granules of toxic chemicals that can digest microorganisms. Basophils, as well as other types of white blood cells, are responsible for the symptoms of allergy.

B CELL LYMPHOMA: See Lymphoma.

B CELLS: See B Lymphocytes.

BDNA TEST: (bDNA) See Branched DNA Assay.

BETA 2 MICROGLOBULIN (B2M): Protein tightly bound to the surface of many nucleated cells, particularly those of the immune

system. Elevated B2M levels occur in a variety of diseases. While elevated B2M is not specific to HIV, there is a correlation between this marker and the progression of HIV disease. See Immune System.

BILIRUBIN: A red pigment occurring in liver bile, blood, and urine. Its measurement can be used as an indication of the health of the liver. Bilirubin is the product of the breakdown of hemoglobin in red blood cells. It is removed from the blood and processed by the liver, which secretes it into the digestive tract. The normal value is 0.1 to 1.5 milligrams per liter of blood. An elevated level of bilirubin in blood serum is an indication of liver disease or drug-induced liver impairment.

BINDING ANTIBODY: As related to HIV infection: An antibody that attaches to some part of HIV. Binding antibodies may or may not adversely affect the virus.

BIOAVAILABILITY: The extent to which an oral medication is absorbed in the digestive tract and reaches the bloodstream.

BIOLOGICAL RESPONSE MODIFIERS (BRMS): Substances, either natural or synthesized, that boost, direct, or restore normal immune defenses. BRMs include interferons (see), interleukins (see), thymus (see), hormones, and monoclonal antibodies (see).

BIOPSY: Surgical removal of a piece of tissue from a living subject for microscopic examination to make a diagnosis (e.g., to determine whether abnormal cells such as cancer cells are present).

BIOTECHNOLOGY: 1. Use of living organisms or their products to make or modify a substance. These include recombinant DNA techniques (genetic engineering; see) and hybridoma technology. 2. Industrial application of the results of biological research, particularly in fields such as recombinant DNA or gene splicing, which permits the production of synthetic hormones or enzymes by combining genetic material from different species.

BLINDED STUDY: A clinical trial in which participants are unaware as to whether they are in the experimental or control arm of the study. See Double Blind Study.

BLOOD-BRAIN BARRIER: A selective barrier (obstacle) between brain blood vessels and brain tissues whose effect is to restrict what may pass from the blood into the brain. Certain compounds readily cross the blood–brain barrier; others are completely blocked.

B LYMPHOCYTES (B CELLS): One of the two major classes of lymphocytes (see), B lymphocytes are blood cells of the immune system, derived from the bone marrow and spleen, and involved in the production of antibodies. During infections, these cells are transformed into plasma cells that produce large quantities of antibody directed at specific pathogens. When antibodies bind to foreign proteins, such as those that occur naturally on the surfaces of bacteria, they mark the foreign cells for consumption by other cells of the immune system. This transformation occurs through interactions with various types of T cells (see) and other components of the immune system. In persons living with AIDS, the functional ability of both the B and the T lymphocytes is damaged, with the T lymphocytes being the principal site of infection by HIV.

BODY FLUIDS: Any fluid in the human body, such as blood, urine, saliva (spit), sputum, tears, semen, mother's milk, or vaginal secretions. Only blood, semen, mother's milk, and vaginal secretions have been linked directly to the transmission of HIV.

BONE MARROW: Soft tissue located in the cavities of the bones where blood cells such as erythrocytes, leukocytes, and platelets (see entries for these terms) are formed.

BONE MARROW SUPPRESSION: A side effect of many anticancer and antiviral drugs, including AZT (see). Leads to a decrease in white blood cells, red blood cells, and platelets. Such reductions, in turn, result in anemia, bacterial infections, and spontaneous or excess bleeding.

BOOSTER: A second or later dose of a vaccine (see) given to increase the immune response to the original dose.

BRANCHED DNA ASSAY: (bDNA test) A test developed by the Chiron Corporation for measuring the amount of HIV (as well as other viruses) in blood plasma. The test uses a method that creates a luminescent signal whose brightness depends on the amount of viral RNA (see) present. Test results are calibrated in numbers of virus particle equivalents per milliliter of plasma. The bDNA test is similar in results but not in technique to the PCR test (see). bDNA testing is currently being used to evaluate the effectiveness of drug treatment regimens and to gauge HIV disease progression. Newer versions, or generations, of these assays are being developed; they will be able to detect smaller numbers of copies of HIV in a blood sample. See Viral Burden.

BREAKTHROUGH INFECTION: An infection, caused by the infectious agent the vaccine is designed to protect against, that occurs during the course of a vaccine trial. These infections may be caused by exposure to the infectious agent before the vaccine has taken effect, or before all doses of the vaccine have been given.

BRONCHOSCOPY: Visual examination of the bronchial passages of the lungs through the tube of an endoscope (usually a curved flexible tube containing fibers that carry light down the tube and project an enlarged image up the tube to the viewer) that is inserted into the upper lungs. Can be used for extraction of material from the lungs. See Endoscopy.

BUDDING: See Assembly and Budding.

BUFFALO HUMP: See Lipodystrophy

BURKITT'S LYMPHOMA: See Lymphoma.

CACHEXIA: General ill health and malnutrition, marked by weakness and emaciation, usually associated with serious disease. See AIDS Wasting Syndrome.

CANDIDA: Yeast-like fungi commonly found in the normal flora of the mouth, skin, intestinal tract, and vagina, which can become clinically infectious in immune-compromised persons. See Candidiasis, Fungus; Thrush.

CANDIDIASIS: An infection with a yeast-like fungus (see) of the Candida family, generally *Candida albicans*. It most commonly involves the skin (dermatocandidiasis), oral mucosa (thrush), respiratory tract (bronchocandidiasis), and vagina (vaginal candidiasis, formerly called monilia). Candidiasis of the esophagus, trachea, bronchi, or lungs is an indicator disease for AIDS. Oral or recurrent vaginal candida infection is an early sign of immune system deterioration. See Opportunistic Infection; Thrush.

CARCINOGEN: Any cancer-producing substance.

CATHETER: A tubular medical device for insertion into canals, vessels, passageways, or body cavities, usually to permit injection (e.g., through an intravenous catheter into a vein), withdrawal of fluids, or to keep a passage open.

CBCT: See Community-Based Clinical Trial.

CBO: See Community-Based Organization.

CCR5: Cell surface molecule, which is needed along with the primary receptor, the CD4 (see) molecule, in order to fuse with the membranes of the immune system cells. Researchers have found that the strains of HIV most often transmitted from person to person require the CCR5

molecule and CD4 molecule in order for HIV to enter the cell. In addition to its role in fusion, CC CKR5 is a receptor for certain immune-signaling molecules called chemokines (see) that are known to suppress HIV infection of cells. See Chemokines, CXCR4.

CDC: See Centers for Disease Control and Prevention.

CD4 (T4) OR CD4+ CELLS: 1. A type of T cell involved in protecting against viral, fungal, and protozoal infections. These cells normally orchestrate the immune response, signaling other cells in the immune system to perform their special functions. Also known as T helper cells. 2. HIV's preferred targets are cells that have a docking molecule called "cluster designation 4" (CD4) on their surfaces. Cells with this molecule are known as CD4-positive (or CD4+) cells. Destruction of CD4+ lymphocytes is the major cause of the immunodeficiency observed in AIDS, and decreasing CD4+ lymphocyte levels appear to be the best indicator for developing opportunistic infections. Although CD4 counts fall, the total T cell level remains fairly constant through the course of HIV disease, due to a concomitant increase in the CD8+ cells. The ratio of CD4+ to CD8+ cells is therefore an important measure of disease progression. See CD8 (T8) Cells; Immunodeficiency.

CD8 (T8) CELLS: A protein embedded in the cell surface of suppressor T lymphocytes (see). Also called cytotoxic T cells (see). Some CD8 cells recognize and kill cancerous cells and those infected by intracellular pathogens (some bacteria, viruses, and mycoplasma). These cells are called cytotoxic T lymphocytes (see).

CDC NATIONAL AIDS HOTLINE: Provides education, information, and referrals for persons living with HIV, their families and friends, health professionals, and the general public on HIV/AIDS issues, including transmission, prevention, and testing. The Hotline number is 1–800–342–AIDS.

CDC NATIONAL PREVENTION INFORMATION NETWORK: The National Prevention Information Network (NPIN) is a national

reference, referral and distribution service for information on HIV/AIDS, STDs (see) and TB (see), sponsored by the Centers for Disease Control and Prevention (CDC) (see). All of the NPIN's services are designed to facilitate sharing of information and resources among people working in HIV, STD, and TB prevention, treatment, and support services. NPIN staff serve a diverse network of people who work in international, national, state, and local settings. **Internet address: http://www.cdcnpin.org/.**

CELL LINES: Specific cell types artificially maintained in the laboratory (i.e., in vitro) for scientific purposes.

CELL-MEDIATED IMMUNITY (CMI): This branch of the immune system exists primarily to deal with viruses that are more insidious than bacteria because they invade the host (e.g., human) cells where they can hide from the antibody-making cells of the immune system. With this system, the reaction to foreign material is performed by specific defense cells, such as killer T cells (see), macrophages (see), and other white blood cells rather than by antibodies.

CELLULAR IMMUNITY: See Cell-Mediated Immunity.

CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC): The U.S. Department of Health and Human Services (see) agency with the mission to promote health and quality of life by preventing and controlling disease, injury, and disability. CDC operates 11 Centers including the National Center for HIV, STD, and TB Prevention (see). CDC assesses the status and characteristics of the HIV epidemic and conducts epidemiologic, laboratory, and surveillance investigations. **Internet address: http://www.cdc.gov/.**

CENTRAL NERVOUS SYSTEM (CNS) DAMAGE: (By HIV infection). The central nervous system is composed of the brain, spinal cord, and the meninges (protective membranes surrounding them). Although monocytes (see) and macrophages (see) can be infected by HIV, they appear to be relatively resistant to killing. However, these

cells travel throughout the body and carry HIV to various organs, especially the lungs and the brain. Persons living with HIV often experience abnormalities in the central nervous system. Investigators have hypothesized that an accumulation of HIV in brain and nerve cells or the inappropriate release of cytokines (see) or toxic byproducts of these cells may be to blame for the neurological manifestations of HIV disease.

CEREBRAL: Pertaining to the cerebrum, the main portion of the brain.

CEREBROSPINAL FLUID (CSF): Fluid that bathes the brain and the spinal cord. A sample of this fluid is often removed from the body for diagnostic purposes by a lumbar puncture (spinal tap).

CERVICAL CANCER: A neoplasm of the uterine cervix that can be detected in the early curable stage by the Papanicolaou (Pap) test. See Cervical Dysplasia; Cervix; Pap Smear.

CERVICAL DYSPLASIA: Abnormality in the size, shape, and organization of adult cells of the cervix (see). Often a precursor lesion for cervical cancer. Studies indicate an increase in prevalence of cervical dysplasia (see) among women living with HIV. Additional studies have documented that a higher prevalence is associated with greater immune suppression. HIV infection also may adversely affect the clinical course and treatment of cervical dysplasia and cancer.

CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN1, CIN2, CIN3): Dysplasia (see) of the cervix (see) epithelium (see), often premalignant (i.e., precancerous), characterized by various degrees of hyperplasia (see), abnormal keratinization (forming horny epidermal tissue), and condylomata. Considerable evidence implicates human papilloma virus (HPV) in the development of CIN. Immunosuppression may also play an important role in facilitating infection or persistence of HPV in the genital tract and progression of HPV-induced neoplasia. See Condyloma; Neoplasm.

CERVIX: The lower, cylindrical terminus of the uterus that juts into the vagina and contains a narrow canal connecting the upper and lower parts of a woman's reproductive tract.

CHALLENGE: In vaccine experiments, the exposure of an immunized animal to the infectious agent.

CHANCROID: A highly contagious sexually transmitted disease caused by the *Hemophilus ducreyi* bacterium. It appears as a pimple, chancre, sore, or ulcer on the skin of the genitals. The lesion appears after an incubation period of 3 to 5 days and may help the transmission of HIV.

CHEMOKINES: Also called beta chemokines. Studies of the relationship between HIV and these immune system chemicals have shown the complex exchanges that take place when HIV and white blood cells meet. Chemokines are intracellular messenger molecules secreted by CD8+ cells (see) whose major function is to attract immune cells to sites of infection. Recent research has shown that HIV-1 needs access to chemokine receptors on the cell surface to infect the cell. Several chemokines—called RANTES, MIP-1A, and MIP-1B—interfere with HIV replication by occupying these receptors. Findings suggest that one mechanism these molecules use to suppress HIV infectivity is to block the process of fusion (see) used by the virus to enter cells.

CHEMOTHERAPY: The treatment, mostly of cancer, using a series of cytotoxic (see) drugs that attack cancerous cells. This treatment commonly has adverse side effects that may include the temporary loss of the body's natural immunity to infections, loss of hair, digestive upset, and a general feeling of illness. Although unpleasant, the adverse effects of treatment are tolerated considering the life-threatening nature of the cancers.

CHLAMYDIA: A sexually transmitted disease (STD, see). The most common sexually transmitted bacterium *(Chlamydia trachomatis)* that infects the reproductive system. In fact, in a 1998 NIAID press release (fact sheet), chlamydia was reported to be the most common STD in the

United States. The infection is frequently asymptomatic (i.e., shows no symptoms), but if left untreated, can cause sterility in women.

CHRONIC IDIOPATHIC DEMYELINATING POLYNEUROPATHY (CIPD): Chronic, spontaneous loss or destruction of myelin. Myelin is a soft, white, somewhat fatty material that forms a thick sheath around the core of myelinated nerve fiber. Patients show progressive, usually symmetric weakness in the upper and lower extremities. Patients with clinical progression of the syndrome (see) after 4 to 6 weeks by definition have CIPD. Treatment in most centers consists of giving IV-immune globulin for 4 to 5 days or plasmapheresis (see) (5 to 6 exchanges over 2 weeks).

CIPD: See Chronic Idiopathic Demyelinating Polyneuropathy.

CIRCULATING IMMUNE COMPLEXES: See Immune Complex.

CIRCUMORAL PARESTHESIA: An abnormal touch sensation, such as burning or prickling around the mouth, often in the absence of an external stimulus. See Paresthesia.

CLADE: Also called a subtype. A clade is a group of related HIV isolates (see Isolate) classified according to their degree of genetic similarity (such as the percentage of identity within their envelope genes). There are currently three groups of HIV–1 isolates: M, N, and O. Isolate M (major strains) consists of at least ten clades, A through J. Group O (outer strains) may consist of a similar number of clades. French researchers reported the discovery of a new HIV–1 isolate that cannot be categorized in either group M or O. The new isolate was found in a Cameroonian woman with AIDS. They suggested that this new isolate be classified as group N (for new or for "non-M-non-O").

CLINICAL: Pertaining to or founded on observation and treatment of patients, as distinguished from theoretical or basic science.

CLINICAL ALERT: The National Institutes of Health (see) in conjunction with the editors of several biomedical journals publish those

bulletins on urgent cases in which timely and broad dissemination of results of clinical trials could prevent morbidity (sickness) and mortality (death). The Clinical Alert does not become a barrier to subsequent publication of the full research paper. Clinical Alerts are widely distributed electronically through the National Library of Medicine (see) and through standard mailings.

CLINICAL ENDPOINT: See Endpoint.

CLINICAL LATENCY: The state or period of an infectious agent, such as a virus or bacterium, living or developing in a host without producing clinical symptoms. Pertaining to HIV infection, infected individuals usually exhibit a period of clinical latency with little evidence of disease, but viral load (see) studies show that the virus is never truly latent (dormant). Even early in the disease, HIV is active within lymphoid organs (see) where large amounts of virus become trapped in the FDC (Follicular Dendritic Cells; see) network. Surrounding tissues are areas rich in CD4+ T cells (see). These cells increasingly become infected and viral particles accumulate both in infected cells and as free virus.

CLINICAL PRACTICE GUIDELINES: Standards for physicians to adhere to in prescribing care for a given condition or illness.

CLINICAL TRIAL: A scientifically designed and executed investigation of the effects of a drug (or vaccine) administered to human subjects. The goal is to define the safety, clinical efficacy, and pharmacological effects (including toxicity, side effects, incompatibilities, or interactions) of the drug. The U.S. government, through the FDA (see), requires strict testing of all new drugs and vaccines prior to their approval for use as therapeutic agents. See entries for Phase I, II, III, and IV Trials.

CLONE: 1. A group of genetically identical cells or organisms descended from a common ancestor. 2. To produce genetically identical copies. 3. A genetically identical replication of a living cell that is valuable for the investigation and reproduction of test cultures.

CMV: See Cytomegalovirus.

CMV RETINITIS: See Cytomegalovirus Retinitis.

CNS: See Central Nervous System.

COCCIDIOIDOMYCOSIS: An infectious fungal disease caused by the inhalation of spores of *Coccidioides immitis,* which are carried on wind-blown dust particles. The disease is endemic in hot, dry regions of the Southwestern United States and Central and South America, and is an opportunistic disease associated with AIDS. Also called desert fever, San Joaquin fever, or Valley fever. See Fungus; Opportunistic Infection.

CODON: A sequence of three nucleotides (see) of messenger RNA that specifies addition of a particular amino acid to, or termination of, a polypeptide chain during protein synthesis. See Ribonucleic Acid.

COFACTORS: 1. Substances, microorganisms, or characteristics of individuals that may influence the progression of a disease or the likelihood of becoming ill. 2. A substance, such as a metallic ion or coenzyme, that must be associated with an enzyme for the enzyme to function. 3. A situation or activity that may increase a person's susceptibility to AIDS. Examples of cofactors are: other infections, drug and alcohol use, poor nutrition, genetic factors, and stress. In HIV immunology, the concept of cofactors is being expanded and new cofactors have been identified. A recent example is the discovery of the interaction of CXCR4 (see) (fusin) and CD4 to facilitate entry of HIV into cells.

COGNITIVE IMPAIRMENT: Loss of the ability to process, learn, and remember information.

COHORT: In epidemiology, a group of individuals with some characteristics in common.

COLITIS: Inflammation of the colon.

COMBINATION THERAPY: (For HIV infection or AIDS). Two or more drugs or treatments used together to achieve optimum results

against HIV infection and/or AIDS. Combination therapy may offer advantages over single-drug therapies by being more effective in decreasing viral load (see). An example of combination therapy would be the use of two nucleoside analog (see) drugs (such as 3TC and AZT; see entries for these drugs) plus either a protease inhibitor (see) or a non-nucleoside reverse transcription inhibitor (see). See Synergism.

COMBIVIR: A combined pill containing Zidovudine (see) and Lamivudine (see) that is FDA approved (09/26/97) for the treatment of HIV infection in adults and adolescents 12 years of age or older.

COMMUNITY-BASED CLINICAL TRIAL (CBCT): A clinical trial conducted primarily through primary-care physicians rather than academic research facilities.

COMMUNITY-BASED ORGANIZATION (CBO): A service organization that provides social services at the local level.

COMMUNITY PLANNING: Community planning groups are responsible for developing comprehensive HIV prevention plans that are directly responsive to the epidemics in their jurisdictions. The goal of HIV Prevention Community Planning is to improve the effectiveness of HIV prevention programs. Together in partnership, representatives of affected populations, epidemiologists, behavioral scientists, HIV/AIDS prevention service providers, health department staff, and others analyze the course of the epidemic in their jurisdiction, determine their priority intervention needs, and identify interventions to meet those needs. CDC (see) supports implementation of an effective planning process.

COMMUNITY PROGRAMS FOR CLINICAL RESEARCH ON AIDS (CPCRA): The CPCRA, founded in 1989, and called the Terry Beirn Community Programs for Clinical Research on AIDS since 1992, is a network of research units composed of community-based health care providers who offer their patients the opportunity to participate in research where they get their health care. The 15 CPCRA units comprise a variety of clinical settings, including private physicians' practices, university, and veterans' hospital clinics; drug treatment centers; and

freestanding community clinics. Patients at these clinics are eligible for participation in CPCRA studies. The CPCRA, funded by the National Institute of Allergy and Infectious Disease (NIAID, see), is targeted to serve populations underrepresented in previous clinical trials efforts. The research focus and scientific agenda of the CPCRA is identifying and improving treatment options in the day-to-day clinical care of people with HIV. **Internet address: http://www.cpcra.org/.**

COMPASSIONATE USE: A method of providing experimental therapeutics (including experimental drugs) prior to final FDA (see) approval for use in humans. This procedure is used with very sick individuals who have no other treatment options. Often, case-by-case approval must be obtained from the FDA for "compassionate use" of a drug or therapy.

COMPLEMENT: A group of proteins in normal blood serum and plasma that, in combination with antibodies (see), causes the destruction of antigens (see), particularly bacteria and foreign blood cells.

COMPLEMENT CASCADE: A precise sequence of events, usually triggered by an antigen-antibody complex, in which each component of the complement system is activated in turn. See Antibodies; Antigen.

COMPLEMENTARY THERAPY: A whole range of services designed to complement traditional medical practice as part of a practitioner's primary care plan for an individual.

CONCOMITANT DRUGS: Drugs that are taken together. Certain concomitant medications may have adverse interactions.

CONCORDE STUDY: Joint French/British clinical trial of AZT in asymptomatic HIV- infected individuals. See AZT.

CONDYLOMA: (*Condyloma acuminatum*). A papilloma (see) with a central core of connective tissue in a treelike structure covered with epithelium (see), usually occurring on the mucous membrane or skin of the external genitals or in the perianal (tissue surrounding the anus) region. Although the lesions are usually few in number, they may

aggregate to form large cauliflower-like masses. Caused by the human papilloma virus (HPV; see), it is infectious and autoinoculable (i.e., capable of being transmitted by inoculation from one part of the body to another). Also called genital warts, venereal warts, or *verruca acuminata.*

CONTAGIOUS: In the context of HIV, has come to be more popularly known as any infectious disease capable of being transmitted by casual contact from person to another. Casual contact can be defined as normal day-to-day contact among people at home, school, or work or in the community. A contagious pathogen (e.g., chicken pox) can be transmitted by casual contact. An infectious pathogen, on the other hand, is transmitted by direct or intimate contact (e.g., sex). HIV is infectious, not contagious.

CONTRAINDICATION: A specific circumstance when the use of certain treatments could be harmful.

CONTROLLED TRIALS: Control is a standard against which experimental observations may be evaluated. In clinical trials, one group of patients is given an experimental drug, while another group (i.e., the control group) is given either a standard treatment for the disease or a placebo (see).

CO-RECEPTORS: A group of proteins that have been found to block the entry of HIV into immune cells.

CORE: The protein capsule surrounding a virus' DNA (see) or RNA (see). In HIV, p55, the precursor molecule to the core, is broken down into the smaller protein molecules p24, p17, p7, and p6. HIV's core is primarily composed of p24 (see).

CORE PROTEIN: See Core.

CORRELATES OF IMMUNITY/CORRELATES OF PROTECTION: The immune responses that protect an individual from a certain disease. The precise identities of the correlates of immunity in HIV are unknown.

CPCRA: See Community Programs for Clinical Research on AIDS.

CREATININE: A protein found in muscles and blood, and excreted by the kidneys in the urine. The level of creatinine in the blood or urine provides a measure of kidney function.

CRIXIVAN: See Indinavir.

CROSS-RESISTANCE: The phenomenon in which a microbe that has acquired resistance to one drug through direct exposure, also turns out to have resistance to one or more other drugs to which it has not been exposed. Cross-resistance arises because the biological mechanism of resistance to several drugs is the same and arises through the identical genetic mutations.

CRYOTHERAPY: The use of liquid nitrogen to freeze and destroy a lesion or growth, sometimes used to induce scar formation and healing to prevent further spread of a condition (e.g., warts or molluscum contagiosum).

CRYPTOCOCCAL MENINGITIS: A life-threatening infection of the membranes (meninges) that line the brain and the spinal cord. Cryptococcal disease is caused by a fungus (*Cryptococcus neoformans*). Most people have been exposed to this organism, which is found in soil contaminated by bird droppings, but it usually does not cause disease in healthy people. The majority of persons with cryptococcal meningitis have immune systems that are damaged by disease, such as AIDS, or suppressed by drugs. The organism can infect almost all organs of the body, although it most commonly causes disease of the meninges, skin, or lungs. See Cryptococcosis.

CRYPTOCOCCOSIS: An infectious disease seen in HIV-infected patients due to the fungus *Cryptococcus neoformans*, which is acquired via the respiratory tract. It can spread from the lungs to the brain, the central nervous system, the skin, the skeletal system, and the urinary tract. See Cryptococcal Meningitis.

CRYPTOSPORIDIOSIS: See Cryptosporidium

CRYPTOSPORIDIUM: The protozoan (see) parasite, *Cryptosporidium parvum,* which causes cryptosporidiosis. The parasite is found in the intestines of animals, and may be transmitted to humans by direct contact with an infected animal, by eating contaminated food, or by drinking contaminated water. The parasite grows in the intestines and may cause severe chronic diarrhea (6–29 bowel movements per day) in people with HIV disease. Cryptosporidiosis usually occurs late in the course of HIV disease as immunological deterioration progresses.

CT SCAN (COMPUTED TOMOGRAPHY SCAN): Radiography (using x-rays) in which a three-dimensional image of a body structure is constructed by computer from a series of cross-sectional images made along an axis. Also referred to as CAT scan. See Magnetic Resonance Imaging (MRI).

CTL: See Cytotoxic T Lymphocyte.

CUTANEOUS: Of, pertaining to, or affecting the skin.

CXCR4: (Also known as Fusin). A cell molecule that acts as a cofactor (see) or co-receptor for the entry of HIV into immune system cells. Early in the epidemic, CD4 (see) molecules were found to be the primary receptor for HIV on immune system cells. Recent data indicate that a second molecule, CXCR4, is also required for fusion and entry of certain strains of HIV into cells. New studies indicate a multistage interplay between HIV and two receptors on white blood cells. After binding to the receptor CD4, the virus fuses with a second receptor, CXCR4, which normally binds to chemokines (see). This double clasp may then signal the receptors to move the virus into the cell.

CYTOKINES: A soluble, hormone-like protein, produced by white blood cells, that acts as a messenger between cells. Cytokines can stimulate or inhibit the growth and activity of various immune cells. Cytokines are essential for a coordinated immune response and can

also be used as immunologic adjuvants. HIV replication is regulated by a delicate balance among the body's own cytokines. By altering that balance one can influence the replication of the virus in the test tube and potentially even in the body. See also Interleukins, Tumor Necrosis Factor.

CYTOMEGALOVIRUS (CMV): A herpes virus that is a common cause of opportunistic diseases in persons with AIDS and other persons with immune suppression. While CMV can infect most organs of the body, persons with AIDS are most susceptible to CMV retinitis (disease of the eye) (see) and colitis (disease of the colon).

CYTOMEGALOVIRUS (CMV) RETINITIS: Most adults in the U.S. have been infected by cytomegalovirus, although the virus usually does not cause disease in healthy people. Because the virus remains in the body for life, it can cause disease if the immune system becomes severely damaged by disease or suppressed by drugs. CMV retinitis is an eye disease common among persons who are living with HIV. Without treatment, persons with CMV retinitis can lose their vision. CMV infection can affect both eyes and is the most common cause of blindness among persons with AIDS.

CYTOPENIA: Deficiency in the cellular elements of the blood.

CYTOPLASM: All of the substance of a cell other than the nucleus.

CYTOTOXIC: An agent or process that is toxic to cells (i.e., it causes suppression of function or cell death).

CYTOTOXIC T LYMPHOCYTE (CTL): A lymphocyte (see) that is able to kill foreign cells marked for destruction by the cellular immune system. CTLs can destroy cancer cells and cells infected with viruses, fungi, or certain bacteria. CTLs are also known as killer T cells; they carry the CD8 marker. CTLs kill virus-infected cells, whereas antibodies (see) generally target free-floating viruses in the blood. See also CD8 (T8) Cells.

DATA SAFETY AND MONITORING BOARD (DSMB): An independent committee, composed of community representatives and clinical research experts, that reviews data while a clinical trial is in progress to ensure that participants are not exposed to undue risk. A DSMB may recommend that a trial be stopped if there are safety concerns or if the trial objectives have been achieved.

DATRI: See Division of AIDS Treatment Research Initiative.

DDC: See Zalcitibine.

DDI: See Didanosine.

DELAVIRDINE: An FDA approved (04/04/97) non-nucleoside reverse transcriptase inhibitor (see) for use in combination with appropriate antiretrovirals when therapy is warranted for treatment of HIV infection. Also called Rescriptor.

DELETION: Elimination of a gene (see) (i.e., from a chromosome) either in nature or in the laboratory.

DEMENTIA: Chronic intellectual impairment (i.e., loss of mental capacity) with organic origins that affects a person's ability to function in a social or occupational setting. See AIDS Dementia Complex.

DEMYELINATION: Destruction, removal, or loss of the myelin (see) sheath of a nerve or nerves.

DENDRITE: Any of the usual branching protoplasmic processes that conduct impulses toward the body of a nerve cell. See Protoplasm.

DENDRITIC CELLS: Patrolling immune system cells that may begin the HIV disease process by carrying the virus from the site of the infection to the lymph nodes (see), where other immune cells become infected.

Dendritic cells travel through the body and bind to foreign invaders—such as HIV—especially in external tissues, such as the skin and the membranes of the gut, lungs, and reproductive tract. They then ferry the foreign substance to the lymph nodes to stimulate T cells (see) and initiate an immune response. In laboratory experiments, the dendritic cells that carry HIV also bind to CD4+ T cells (see), thereby allowing HIV to infect the CD4+ T cells. CD4+ T cells are the primary immune system cells targeted by HIV and depleted during HIV infection.

DEOXYRIBONUCLEIC ACID (DNA): The molecular chain found in genes within the nucleus of each cell, which carries the genetic information that enables cells to reproduce. DNA is the principal constituent of chromosomes, the structures that transmit hereditary characteristics.

DEPARTMENT OF HEALTH AND HUMAN SERVICES (DHHS): The U.S. government's principal agency for protecting the health of all Americans and providing essential human services, especially for those who are least able to help themselves. DHHS includes more than 300 programs, covering a wide spectrum of activities. The Department's programs are administered by 11 operating divisions such as the Centers for Disease Control and Prevention, the Food and Drug Administration and the National Institutes of Health (see the entries for these agencies). DHHS works closely with state and local governments, and many DHHS-funded services are provided at the local level by state or county agencies, or through private-sector grantees. **Internet address: http://www.hhs.gov/.**

DESENSITIZATION: Gradually increasing the dose of a medicine in order to overcome severe reactions. Desensitization procedures have become popular when administering Bactrim to persons with a history of adverse reactions to the drug. Bactrim (see TMP/SMX) is an important drug against PCP (see) infection.

D4T: See Stavudine.

DHHS: See U.S. Department of Health and Human Services.

DIABETES MELLITUS: A metabolic disease in which carbohydrate utilization is reduced and that of lipid and protein utilization is enhanced. Diabetes mellitus occurs when the body produces little or no insulin, or cannot use the insulin that is produced. As a result, unused glucose collects in the blood; this leads to high blood-sugar levels. Insulin is the hormone that allows glucose to leave the bloodstream and enter body cells, where it is used for energy generation or stored for future use. Diabetes mellitus can also lead to long-term complications that include the development of neuropathy (swelling and wasting of the nerves) retinopathy (non-swelling eye disorder), nephropathy (swelling or breakdown disorder of the kidneys) generalized degenerative changes in large and small blood vessels, and increased susceptibility to infections. As related to HIV: In June 1997, the FDA sent a Public Health Advisory letter to health care professionals to report that cases of new onset diabetes mellitus, hyperglycemia (see) or worsening of existing diabetes mellitus were occurring in HIV-infected patients receiving protease inhibitors (see).

DIAGNOSIS: The determination of the presence of a specific disease or infection, usually accomplished by evaluating clinical symptoms and laboratory tests.

DIARRHEA: Uncontrolled, loose, and frequent bowel movements. In the U.S., almost all persons living with AIDS develop diarrhea at some time in the course of their disease. Severe or prolonged diarrhea can lead to weight loss and malnutrition. The excessive loss of fluid that may occur with AIDS-related diarrhea can be life threatening. There are many possible causes of diarrhea in persons who have AIDS. The most common infectious organisms causing AIDS-related diarrhea include cytomegalovirus (CMV; see); the parasites Cryptosporidium, Microsporidia, and *Giardia lamblia;* and the bacteria *Mycobacterium avium* and *Mycobacterium intracellulare*. Other bacteria and parasites that cause diarrheal symptoms in otherwise healthy people may cause more severe, prolonged, or recurrent diarrhea in persons with HIV or AIDS. See Giardiasis; Microsporidiosis; Mycobacterium avium complex (MAC).

DIDANOSINE: A nucleoside reverse transcriptase inhibitor (see) first approved by FDA in 1991 and used for the treatment of HIV infection when antiretroviral therapy is warranted. Also called ddI, Videx.

DIDEOXYCYTIDINE: See Zalcitabine.

DIPLOPIA: Double vision.

DISSEMINATED: Spread (of a disease) throughout the body.

DNA: See Deoxyribonucleic Acid.

DOMAIN: A region of a gene or gene product. See Gene.

DORMANCY: See Latency.

DOSE-RANGING STUDY: A clinical trial (see) in which two or more doses of an agent (such as a drug) are tested against each other to determine which dose works best and is least harmful.

DOSE-RESPONSE RELATIONSHIP: The relationship between the dose of some agent (such as a drug), or the extent of exposure, and a physiological response. A dose-response effect means that as the dose increases, so does the effect.

DOUBLE-BLIND STUDY: A clinical trial (see) design in which neither the participating individuals nor the study staff know which patients are receiving the experimental drug and which are receiving a placebo (see) or another therapy. Double-blind trials are thought to produce objective results, since the expectations of the doctor and the patient about the experimental drug do not affect the outcome. See Blinded Study.

DRUG-DRUG INTERACTION: A modification of the effect of a drug when administered with another drug. The effect may be an increase or a decrease in the action of either substance, or it may be an adverse effect that is not normally associated with either drug.

DRUG RESISTANCE: The ability of some disease-causing microorganisms, such as bacteria, viruses, and mycoplasma, to adapt themselves, to grow, and to multiply even in the presence of drugs that usually kill them. See Cross-Resistance.

DSMB: See Data Safety and Monitoring Board.

DYSPLASIA: Any abnormal development of tissues or organs. In pathology, alteration in size, shape, and organization of adult cells.

DYSPNEA: Difficult or labored breathing.

EDEMA: An abnormal swelling resulting from the accumulation of fluid in the spaces between tissues.

EFAVIRENZ: An FDA approved (09/18/98) non-nucleoside reverse transcriptase inhibitor (see) for combination use with other antiretroviral agents (see) for adults and children with HIV infection. Also called Sustiva.

EFFICACY: (Of a drug or treatment). The maximum ability of a drug or treatment to produce a result regardless of dosage. A drug passes efficacy trials if it is effective at the dose tested and against the illness for which it is prescribed. In the procedure mandated by the FDA, Phase II clinical trials (see) gauge efficacy, and Phase III trials (see) confirm it.

ELISA: (Enzyme-Linked Immunosorbent Assay). A type of enzyme immunoassay (EIA) to determine the presence of antibodies (see) to HIV in the blood or oral fluids. Repeatedly reactive (i.e., two or more) ELISA test results should be validated with an independent supplemental test of high specificity. In the U.S. the validation test used most often is the Western Blot (see) test.

EMPIRICAL: Based on experimental data, not on a theory.

ENCEPHALITIS: A brain inflammation of viral or other microbial origin. Symptoms include headaches, neck pain, fever, nausea, vomiting, and nervous system problems. Several types of opportunistic infections can cause encephalitis.

ENDEMIC: Pertaining to diseases associated with particular locales or population groups.

ENDOGENOUS: Relating to or produced by the body.

ENDOSCOPY: Viewing the inside of a body cavity (e.g., colon) with an endoscope, a device using flexible fiber optics.

ENDOTOXIN: A toxin present inside a bacterial cell.

ENDPOINT: A category of data used to compare the outcome in different arms of a clinical trial. Common endpoints are severe toxicity, disease progression, or—especially in HIV disease—surrogate markers, such as CD4 (see) count; sometimes death is used as an endpoint. The term is confusing because it often incorrectly implies that patients in a study are no longer followed after they experience an endpoint. This is obviously true where the event is death, but need not be so for nonfatal events. In fact, the design of the trial may require continued treatment and follow-up of patients over the entire course of the trial, regardless of the number of nonfatal "endpoints" observed.

END-STAGE DISEASE: Final period or phase in the course of a disease leading to a person's death.

ENTERIC: Pertaining to the intestines.

ENTERITIS: Inflammation of the intestine.

ENV: *(env)* A gene (see) of HIV that codes for the protein gp160, the precursor of the envelope proteins gp120 and gp41. See gp160; gp120; gp41.

ENVELOPE: In virology, a protein covering that packages the virus's genetic information. The outer coat, or envelope, of HIV is composed of two layers of fat-like molecules called lipids (see) taken from the membranes of human cells. Embedded in the envelope are numerous cellular proteins, as well as mushroom-shaped HIV proteins that protrude from the surface. Each mushroom is thought to consist of a cap made of four glycoprotein (see) molecules called gp120 (see), and a stem consisting of four gp41 (see) molecules embedded in the envelope. The virus uses these proteins to attach to and infect cells.

ENZYME: A cellular protein whose shape allows it to hold together several other molecules in close proximity to each other. In this way, enzymes are able to induce chemical reactions in other substances with little expenditure of energy and without being changed themselves. Basically, an enzyme acts as a catalyst.

EOSINOPHIL: A type of white blood cell, called granulocyte, that can digest microorganisms. The granules can be stained by the acid dye, eosin, for microscopic examination.

EOSINOPHILLIC FOLLICULITIS: An inflammatory reaction around hair follicles, characterized by very itchy papules (small elevation or bump on the skin) that may grow together to form plaques. The cause of this condition in persons with AIDS has yet to be established; it involves invasion of the follicles by eosinophils (see). Partially successful treatment has been reported with ultraviolet light, steroids, antihistamines, and itraconazole.

EPIDEMIC: A disease that spreads rapidly through a demographic segment of the human population, such as everyone in a given geographic area; a military base, or similar population unit; or everyone of a certain age or sex, such as the children or women of a region. Epidemic diseases can be spread from person to person or from a contaminated source such as food or water.

EPIDEMIOLOGIC SURVEILLANCE: The ongoing and systematic collection, analysis, and interpretation of data about a disease or health condition. As part of a surveillance system to monitor the HIV epidemic in the U.S., the Centers for Disease Control and Prevention (CDC) (see), in collaboration with state and local health departments, other federal agencies, blood collection agencies, and medical research institutions, conducts standardized HIV seroprevalence (see) surveys in designated subgroups of the U.S. population. Collecting blood samples for the purpose of surveillance is called serosurveillance.

EPIDEMIOLOGY: The branch of medical science that deals with the study of incidence and distribution and control of a disease in a population.

EPITHELIUM: The covering of the internal and external organs of the body. Also the lining of vessels, body cavities, glands, and organs. It consists of cells bound together by connective material and varies in the number of layers and the kinds of cells.

EPITOPE: A unique shape or marker carried on an antigen's surface that triggers a corresponding antibody response. See Antibodies; Antigen.

EPIVIR: See Lamivudine.

EPSTEIN–BARR VIRUS (EBV): A herpes-like virus that causes one of the two kinds of mononucleosis (the other is caused by CMV, see). It infects the nose and throat and is contagious. EBV lies dormant in the lymph glands and has been associated with Burkitt's lymphoma (see) and hairy leukoplakia (see).

ERYTHEMA: Redness or inflammation of the skin or mucous membranes.

ERYTHEMA MULTIFORME: A skin disease characterized by papular (small, solid, usually conic elevation of the skin) or vesicular lesions (blisters), and reddening or discoloration of the skin often in concentric zones about the lesion (see). Associated with many infections, collagen disease, drug sensitivities, allergies, and pregnancy. A severe form of this condition is Stevens–Johnson Syndrome (see).

ERYTHROCYTES: Red blood cells whose major function is to carry oxygen to cells.

ETIOLOGY: The study or theory of the factors that cause disease.

EXCLUSION/INCLUSION CRITERIA: The medical or social standards determining whether a person may or may not be allowed to enter a clinical trial. For example, some trials may not include persons with chronic liver disease, or may exclude persons with certain drug allergies; others may exclude men or women or only include persons with a lowered T cell count.

EXOGENOUS: Developed or originating outside the body.

EXOTOXIN: A toxic substance, made by bacteria released outside the bacterial cell.

EXPANDED ACCESS: Refers to any of the FDA (see) procedures, such as compassionate use, parallel track, and treatment IND (see), that distribute experimental drugs to patients who are failing on currently available treatments for their condition and also are unable to participate in ongoing clinical trials.

EXPERIMENTAL DRUG: A drug that is not FDA licensed for use in humans, or as a treatment for a particular condition. See also off-label use.

EXPRESSION SYSTEM: In HIV vaccine production, cells into which an HIV gene has been inserted to produce desired HIV proteins.

FALLOPIAN TUBES: Part of the female reproductive system. A pair of ducts opening at one end into the uterus and at the other end into the peritoneal cavity, over the ovary. Each tube serves as a passage through which the ovum (egg) is carried to the uterus and through which spermatozoa (sperm) move out toward the ovary.

FDA: See Food and Drug Administration.

FDC: See Follicular Dendritic Cells.

FLOATERS: Drifting dark spots within the field of vision. Floaters can be caused by infection with Cytomegalovirus (CMV) retinitis (see), but also can appear in persons as a normal part of the aging process.

FOLIC ACID: A crystalline vitamin of the B complex that is used especially in the treatment of nutritional anemias. It occurs in green plants, fresh fruit, liver, and yeast. Also called folacin, folate, and vitamin B9.

FOLINIC ACID: Also called citrovorum factor. A metabolically active form of folic acid (see) that has been used in cancer therapy to protect normal cells against methotrexate—a cancer chemotherapy agent. Also used to treat megaloblastic anemias.

FOLLICLE: A small anatomical sac, cavity, or deep narrow-mouthed depression (e.g., a hair follicle).

FOLLICULAR DENDRITIC CELLS (FDCS): Cells found in the germinal centers of lymphoid organs. FDCs have thread-like tentacles that form a weblike network to trap invaders and present them to other cells of the immune system for destruction. See Lymphoid Organs.

FOMITE: An inanimate object that can harbor pathogenic microorganisms and thus serve as an agent of transmission of an infection.

FOOD AND DRUG ADMINISTRATION (FDA): The U.S. Department of Health and Human Services (see) agency responsible for ensuring the safety and effectiveness of all drugs, biologics, vaccines, and medical devices, including those used in the diagnosis, treatment, and prevention of HIV infection, AIDS, and AIDS-related opportunistic infections. The FDA also works with the blood banking industry to safeguard the nation's blood supply. **Internet address: http://www.fda.gov/.**

FORTOVASE: See Saquinavir.

FUNCTIONAL ANTIBODY: An antibody (see) that binds to an antigen (see) and has an effect. For example, neutralizing antibodies inactivate HIV or prevent it from infecting other cells.

FUNGUS: 1. One of a group of primitive, nonvascular organisms including mushrooms, yeasts, rusts, and molds. 2. Fungi, which were once classified as plants, have since been reclassified as unmoving organisms that lack chlorophyll. Some fungi are single-celled but differ from bacteria in that they have a distinct nucleus and other cellular structures. Reproduction is accomplished by spores. Mycologists (scientists working with fungi) estimate that there are 100,000 species of fungi, ranging from baker's yeast to dermatophytes (fungi that cause ringworm and athlete's foot) to potentially invasive species such as *Candida albicans* and *Aspergillus*. As many as 150 of these organisms have now been linked to animal or human diseases.

FUSIN: (See CXCR4).

FUSION INHIBITOR: A class of antiretroviral agents that binds to the gp41 (see) envelope protein and blocks the structural changes necessary for the virus to fuse with the host CD4 cell (see). When the

virus cannot penetrate the host cell membrane and infect the cell, HIV replication within that host cell is prevented.

FUSION MECHANISM: Fusion is an integral step in the process whereby HIV enters cells. Researchers have found that in addition to the primary receptor, the CD4 (see) molecule, other cofactors, such as CCR5 (see) and CXCR4 (see), are needed in order for HIV to fuse with the membranes of the immune system cells.

GAG: *(gag)* A gene of HIV that codes for the core protein p55. p55 is the precursor of HIV proteins p17, p24, p7, and p6. These form HIV's capsid (see nucleocapsid), the inner protein shell surrounding HIV's strand of RNA.

GAMMA GLOBULIN: One of the proteins in blood serum that contains antibodies. Passive immunizing agents obtained from pooled human plasma. See Globulins, Immunoglobulins.

GAMMA INTERFERON: A T cell-derived stimulating substance that suppresses virus reproduction, stimulates other T cells (see), and activates macrophage (see) cells.

GANGLION: A mass of nervous tissue, composed principally of nerve-cell bodies, usually lying outside the central nervous system (see).

GASTROINTESTINAL (GI): Relating to the stomach and intestines.

GENE: 1. A unit of DNA (see) that carries information for the biosynthesis of a specific product in the cell. 2. Ultimate unit by which inheritable characteristics are transmitted to succeeding generations in all living organisms. Genes are contained by, and arranged along the length of, the chromosome. The gene is composed of deoxyribonucleic acid (DNA). Each chromosome of each species has a definite number and arrangement of genes, which govern both the structure and metabolic functions of the cells and thus of the entire organism. They provide information for the synthesis of enzymes and other proteins and specify when these substances are to be made. Alteration of either gene number or arrangement can result in mutation (a change in the inheritable traits).

GENE THERAPY: Any of a number of experimental treatments in which cell genes (see) are altered. Some gene therapies attempt to provoke new immune activity; some try to render cells resistant to infection; some involve the development of enzymes that destroy viral or cancerous genetic material within cells.

GENETIC ENGINEERING: The technique by which genetic material from one organism is inserted into a foreign cell in order to mass-produce the protein encoded by the inserted genes. This relatively new technique manipulates the DNA (genetic material) of cells. For example, in this technique, the genes, which are actually portions of molecules of DNA, are removed from the donor organism (insect, plant, mammal, or other organism) and spliced into the genetic material of a virus; the virus is then allowed to infect recipient bacteria. In this way the bacteria become recipients of both viral and foreign genetic material. When the virus replicates within the bacteria, large quantities of the foreign as well as viral material are made. (See also Recombinant).

GENITAL ULCER DISEASE: Ulcerative lesions on the genitals usually caused by a sexually transmitted disease such as herpes, syphilis, or chancroid. The presence of genital ulcers may increase the risk of transmitting HIV.

GENITAL WARTS: See Condyloma.

GENITOURINARY TRACT: The organs concerned with the production and excretion of urine and those concerned with reproduction. Also called genitourinary system, urogenital system, or urogenital tract.

GENOME: The complete set of genes (see) in the chromosomes (see) of each cell of a particular organism.

GENOTYPIC ASSAY: A test that determines if HIV has become resistant to the antiviral drug(s) the patient is currently taking. The test analyzes a sample of the virus from the patient's blood to identify any

mutations (see) in the virus that are associated with resistance (see) to specific drugs.

GERMINAL CENTERS: One of a series of follicles or cavities around the periphery of lymph nodes. Germinal centers are the site of antibody production and are populated mostly by B cells but include a few T cells (see) and macrophages (see). As HIV infection progresses, the germinal centers gradually decay.

GIARDIASIS: A common protozoal infection of the small intestine, spread via contaminated food and water and direct person-to-person contact. See Diarrhea.

GLOBULINS: Simple proteins found in the blood serum, which contain various molecules central to the immune system function. See Immunoglobulin.

GLYCOPROTEIN: A conjugated protein in which the nonprotein group is a carbohydrate (i.e., a sugar molecule); also called glucoprotein.

GONORRHEA: An infection caused by *Neisseria gonorrhoeae* (bacteria from the family Neisseriaceae containing gram-negative cocci). Although gonorrhea is considered primarily a sexually transmitted disease (see), it can also be transmitted to newborns during the birth process.

GP41: *(gp41)* Glycoprotein 41, a protein embedded in the outer envelope (see) of HIV. Plays a key role in HIV's infection of CD4+ T cells (see) by facilitating the fusion of the viral and the cell membranes. See gp120.

GP120: *(gp120)* Glycoprotein 120, a protein that protrudes from the surface of HIV and binds to CD4+ T cells (see). In a two-step process that allows HIV to breach the membrane of T cells (see), gp120-CD4 complex refolds to reveal a second structure that binds to CCR5 (see),

one of several chemokine (see) co-receptors used by the virus to gain entry into T cells.

GP160: *(gp160)* Glycoprotein 160, a precursor of HIV envelope proteins gp41 and gp120 (see).

GRANULOCYTE: A type of white blood cell filled with granules of compounds that digest microorganisms. Granulocytes are part of the innate immune system (see) and have broad-based activity. They do not respond only to specific antigens as do B cells (see) and T cells (see). Basophils (see), eosinophils (see), and neutrophils (see) are all granulocytes.

GRANULOCYTE-COLONY STIMULATING FACTOR (G-CSF): A cytokine (see) that stimulates the growth of granulocytes (see), a type of white blood cell. G-CSF alleviates the neutropenia (see) that is a side effect of certain drugs.

GRANULOCYTE MACROPHAGE-COLONY STIMULATING FACTOR (GM-CSF): A cytokine (see) that stimulates the growth of granulocytes (see) and macrophages (see). Like the granulocyte-colony stimulating factor (G-CSF, see), GM-CSF alleviates neutropenia (see) but is less specific and has more side effects than G-CSF.

GRANULOCYTOPENIA: A lack or low level of granulocytes (see) in the blood. Often used interchangeably with neutropenia.

HAART: See Highly Active Antiretroviral Therapy.

HAIRY LEUKOPLAKIA: See Oral Hairy Leukoplakia.

HALF-LIFE: The time required for half the amount of a drug to be eliminated from the body.

HCFA: See Health Care Financing Administration.

HEALTH CARE FINANCING ADMINISTRATION (HCFA): The federal agency that administers the Medicare, Medicaid, and Child Health Insurance Programs. **Internet address: http://www.hcfa.gov/.**

HEALTH RESOURCES AND SERVICES ADMINISTRATION (HRSA): A U.S. Department of Health and Human Services (see) agency that directs national health programs which improve the health of the Nation by assuring quality health care to underserved, vulnerable, and special-need populations and by promoting appropriate health professions workforce capacity and practice, particularly in primary care and public health. Among other functions, HRSA administers the Ryan White C.A.R.E. Act (see) Titles I, II, III(b), IV, SPNS, and AETCs (see explanations for these terms under Ryan White C.A.R.E. Act) to provide treatment and services for those affected by HIV/AIDS. HRSA administers programs to demonstrate how communities can organize their health care resources to develop an integrated, comprehensive, culturally competent system to care for those with AIDS and HIV infection. HRSA also administers education and training programs for health care providers and community service workers who care for persons living with HIV or AIDS. **Internet address: http://www.hrsa.dhhs.gov/.**

HELPER/SUPPRESSOR RATIO (OF T CELLS): T cells are lymphocytes (white blood cells; see) that are formed in the thymus (see) and

are part of the immune system. They have been found to be abnormal in persons with AIDS. The normal ratio of helper T cells (CD4+ cells; see) to suppressor T cells (CD8+ cells; see) is approximately 2:1. This ratio becomes inverted in persons with AIDS but also may be abnormal for a host of other temporary reasons.

HELPER T CELLS: Lymphocytes (see) bearing the CD4 marker that are responsible for many immune system functions, including turning antibody production on and off.

HEMATOCRIT: A laboratory measurement that determines the percentage of packed red blood cells in a given volume of blood. In women, red blood cells are normally 37 to 47 percent of their blood, and in men, red blood cells are normally 40 to 54 percent of their blood.

HEMATOTOXIC: Poisonous to the blood or bone marrow.

HEMOGLOBIN: The component of red blood cells that carries oxygen.

HEMOLYSIS: The rupture of red blood cells.

HEMOPHILIA: An inherited disease that affects mostly males and prevents normal blood clotting. It is treated by lifelong injections of a synthetic version of the clotting factor lacking in persons with the disease. The new recombinant (see) clotting factor replaces the natural product, which was extracted from people's blood and, when not heat treated, could carry HIV.

HEPATIC: Pertaining to the liver.

HEPATITIS: An inflammation of the liver. May be caused by bacterial or viral infection, parasitic infestation, alcohol, drugs, toxins, or transfusion of incompatible blood. Although many cases of hepatitis are not a serious threat to health, the disease can become chronic and can sometimes lead to liver failure and death. There are four major types of viral hepatitis: (1) hepatitis A, caused by infection with the hepatitis A virus, which is spread by fecal-oral contact; (2) hepatitis B, caused by infection with the hepatitis B virus (HBV), which is most commonly passed on

to a partner during intercourse, especially during anal sex, as well as through sharing of drug needles; (3) non-A, non-B hepatitis, caused by the hepatitis C virus, which appears to be spread through sexual contact as well as through sharing of drug needles (another type of non-A, non-B hepatitis is caused by the hepatitis E virus, principally spread through contaminated water); (4) delta hepatitis, which occurs only in persons who are already infected with HBV and is caused by the HDV virus; most cases of delta hepatitis occur among people who are frequently exposed to blood and blood products such as persons with hemophilia (see).

HEPATOMEGALY: Enlargement of the liver.

HERPES VIRUSES: A group of viruses that includes herpes simplex type 1 (HSV–1), herpes simplex type 2 (HSV–2), cytomegalovirus (CMV), Epstein-Barr virus (EBV), varicella zoster virus (VZV), human herpes virus type 6 (HHV–6), and HHV–8, a herpes virus associated with Kaposi's Sarcoma (see). See entries under names of some of the individual viruses.

HERPES SIMPLEX VIRUS I (HSV–I): A virus that causes cold sores or fever blisters on the mouth or around the eyes, and can be transmitted to the genital region. Stress, trauma, other infections, or suppression of the immune system can reactivate the latent virus.

HERPES SIMPLEX VIRUS II (HSV–II): A virus causing painful sores of the anus or genitals that may lie dormant in nerve tissue. It can be reactivated to produce the symptoms. HSV–II may be transmitted to a neonate (newborn child) during birth from an infected mother, causing retardation and/or other serious complications. HSV–II is a precursor of cervical cancer (see).

HERPES VARICELLA ZOSTER VIRUS (VZV): The varicella virus causes chicken pox in children and may reappear in adults as herpes zoster. Also called shingles, herpes zoster consists of very painful blisters on the skin that follow nerve pathways.

HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART): The name given to treatment regimens recommended by leading HIV experts to aggressively suppress viral replication (see) and progress of HIV disease. The usual HAART regimen combines three or more different drugs such as two nucleoside reverse transcriptase inhibitors (NRTIs, see) and a protease inhibitor (see), two NRTIs and a non-nucleoside reverse transcriptase inhibitor (NNRTI, see) or other combinations. These treatment regimens have been shown to reduce the amount of virus so that it becomes undetectable in a patient's blood. For information about the U.S. Public Health Service recommendations for the treatment of HIV infections in adults, adolescents, children, and pregnant women, call the HIV/AIDS Treatment Information Service at 1–800–448–0440. **Internet address: http://www.hivatis.org/.**

HISTOCOMPATIBILITY TESTING: A method of matching the self-antigens on the tissues of a transplant donor with those of a recipient. The closer the match, the better the chance that the transplant will not be rejected. See Human Leukocyte Antigens.

HISTOPLASMOSIS: A fungal infection, commonly of the lungs, caused by the fungus *Histoplasma capsulatum*. This fungus is commonly found in bird and/or bat droppings in the Ohio and Mississippi Valley region, the Caribbean Islands, and in Central and South America. It is spread by breathing in the spores of the fungus. The most definitive test for the fungus has been from fungal stains and bone marrow cultures. Blood testing has proved to be less reliable. In areas where *H. capsulatum* is prevalent, 80 percent or more of the population has been exposed to infection through breathing in airborne spores produced by the fungus. Persons with severely damaged immune systems, such as those with AIDS, are vulnerable to a very serious disease known as progressive disseminated histoplasmosis. Nationwide, about 5 percent of persons with AIDS have histoplasmosis, but in geographic areas where the fungus is common, persons with AIDS are at high risk for disseminated histoplasmosis.

HIV–1: See Human Immunodeficiency Virus Type 1.

HIV-2: See Human Immunodeficiency Virus Type 2.

HIV DISEASE: During the initial infection with HIV, when the virus comes in contact with the mucosal surface, and finds susceptible T cells (see T lymphocytes), the first site at which there is truly massive production of the virus in lymphoid tissue. This leads to a burst of massive viremia (see) with wide dissemination of the virus to lymphoid organs. The resulting immune response to suppress the virus is only partially successful and some virus escapes. Eventually, this results in high viral turnover that leads to destruction of the immune system. HIV disease is, therefore, characterized by a gradual deterioration of immune functions. During the course of infection, crucial immune cells, called CD4+ T cells (see), are disabled and killed, and their numbers progressively decline. See Acquired Immunodeficiency Syndrome; Human Immunodeficiency Virus Type 1.

HIV-RELATED TUBERCULOSIS: See Tuberculosis.

HIV SET POINT: The rate of virus replication that stabilizes and remains at a particular level in each individual after the period of primary infection.

HIV VIRAL LOAD: See Viral Load.

HIVID: See Zalcitabine.

HLA: See Human Leukocyte Antigens.

HODGKIN'S DISEASE: A progressive malignant cancer of the lymphatic system. Symptoms include lymphadenopathy, wasting, weakness, fever, itching, night sweats, and anemia. Treatment includes radiation and chemotherapy. See Lymphoma.

HOLISTIC MEDICINE: Healing traditions that promote the protection and restoration of health through theories reputedly based on the body's natural ability to heal itself and through manipulation of various ways body components affect each other and are influenced by the external environment.

HOMOLOGOUS: Similar in appearance or structure, but not necessarily in function.

HORMONE: An active chemical substance formed in one part of the body and carried in the blood to other parts of the body where it stimulates or suppresses cell and tissue activity. See Pituitary Gland.

HOST: A plant or animal harboring another organism.

HOST FACTORS: The body's potent mechanisms for containing HIV, including immune system cells called CD8+ T cells (see), which may prove more effective than any antiretroviral (see) drug in controlling HIV infection.

HPV: See Human Papilloma Virus.

HRSA: See Health Resources and Services Administration.

HTLV-I: See Human T Cell Lymphotropic Virus Type I.

HTLV-II: See Human T Cell Lymphotropic Virus Type II.

HUMAN GROWTH HORMONE (HGH): A peptide hormone secreted by the anterior pituitary gland in the brain. HGH enhances tissue growth by stimulating protein formation. A recombinant (genetically engineered) HGH, called Serostim, has been approved by FDA as a treatment for AIDS wasting syndrome (see).

HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 (HIV-1): 1. The retrovirus isolated and recognized as the etiologic (i.e., causing or contributing to the cause of a disease) agent of AIDS. HIV–1 is classified as a lentivirus in a subgroup of retroviruses. 2. Most viruses and all bacteria, plants, and animals have genetic codes made up of DNA (see), which uses RNA (see) to build specific proteins. The genetic material of a retrovirus such as HIV is the RNA itself. HIV inserts its own RNA into the host cell's DNA, preventing the host cell from carrying out its natural functions and turning it into an HIV factory. See Lentivirus; Retrovirus.

HUMAN IMMUNODEFICIENCY VIRUS TYPE 2 (HIV-2): A virus closely related to HIV–1 that has also been found to cause AIDS. It was first isolated in West Africa. Although HIV–1 and HIV–2 are similar in their viral structure, modes of transmission, and resulting opportunistic infections (see), they have differed in their geographic patterns of infection.

HUMAN LEUKOCYTE ANTIGENS (HLA): Marker molecules on cell surfaces that identify cells as "self" and prevent the immune system (see) from attacking them.

HUMAN PAPILLOMA VIRUS (HPV): The virus that causes genital warts and is linked to cervical dysplasia and cervical cancer (see). HPV affects more than 24 million Americans, and CDC (see) estimates that there are at least 500,000 new cases each year. There is no specific cure for an HPV infection, but the warts can be removed or controlled by podophyllotoxin, the active ingredient in podophyllin. Interferon is used in the treatment of refractory or recurrent genital warts. Cryotherapy, laser treatment, or conventional surgery can remove the warts. The virus can be transmitted through sexual contact. HPV is a frequently seen infection in women with HIV/AIDS.

HUMAN T CELL LYMPHOTROPIC VIRUS TYPE I (HTLV–I): HTLV–I and HTLV–II (see), like all retroviruses (see), are single-stranded RNA (see) viruses containing a genome that replicates through a DNA (see) intermediate or intermediary. This unique life cycle is made possible by the presence of a virally encoded enzyme, reverse transcriptase (see), which converts a single-stranded viral RNA into a double-stranded DNA provirus that can then be integrated into the host genome. HTLV–I has an affinity for T lymphocytes; it appears to be the causative agent of certain T cell leukemias, T cell lymphomas (see), and HTLV–I-associated myelopathy/tropical spastic paraparesis (HAM/TSP).

HUMAN T CELL LYMPHOTROPIC VIRUS TYPE II (HTLV–II): A virus closely related to HTLV–I (see), shares 60 percent genomic

homology (structural similarity) with HTLV–I. Found predominantly in IV drug users and Native Americans, as well as Caribbean and South American Indian groups. HTLV–II has not been clearly been linked to any disease, but has been associated with several cases of myelopathy/tropical spastic paraparesis (HAM/TSP)-like neurological disease.

HUMORAL IMMUNITY: The branch of the immune system that relies primarily on antibodies (see). See Cell-Mediated Immunity.

HYBRID: An offspring produced from mating plants or animals from different species, varieties, or genotypes.

HYBRIDOMA: A hybrid (see) cell produced by the fusion of an antibody-producing lymphocyte (see) with a tumor cell. Hybridomas are used in the production of monoclonal antibodies (see).

HYDROXYUREA: An inexpensive prescription drug used for the treatment of sickle-cell anemia and some forms of leukemia. Recent treatment studies have shown that hydroxyurea can boost the antiretroviral (see) effects of the anti-HIV drug ddI (see) and possibly of other antiretroviral drugs in HIV-infected people. Since hydroxyurea affects a human host cells' enzyme (see), rather than an HIV enzyme, there may be less chance for the development of resistant virus strains. Although viral load (see) may be reduced significantly in patients on regimens containing hydroxyurea, increases of CD4 cells (see) may be small because of hydroxyurea's suppressive effect on the bone marrow. This can cause neutropenia (presence of abnormally small numbers of white blood cells in the circulating blood, see) or lymphopenia (see).

HYPERGAMMAGLOBULINEMIA: Abnormally high levels of immunoglobulins (see) in the blood. Common in persons with HIV.

HYPERGLYCEMIA: An abnormally high concentration of glucose in the circulating blood, seen especially in patients with diabetes mellitus (see).

HYPERPLASIA: Abnormal increase in the elements composing a part (as tissue cells).

HYPERTHERMIA: An unproven and dangerous experimental procedure that involves temporarily heating a patient's body core to temperatures of up to 108° F on the theory that this temperature kills free HIV and HIV-containing cells. One method for accomplishing this is by passing patients' blood through an external heater. This is called extracorporeal whole body hyperthermia.

HYPOGAMMAGLOBULINEMIA: Abnormally low levels of immunoglobulins (see). See Antibodies.

HYPOTHESIS: A specific statement or proposition, stated in a testable (researchable) form, predicting a particular relationship among multiple variables.

HYPOXIA: Reduction of oxygen supply to tissues.

IDIOPATHIC: Without a known cause.

IDIOPATHIC THROMBOCYTOPENIA PURPURA (ITP): See mmune Thrombocytopenic Purpura.

IDIOTYPES: The unique and characteristic parts of an antibody's variable region, which can themselves serve as antigens. See Antibodies; Antigen.

IHS: See Indian Health Service.

IMMUNE COMPLEX: Clusters formed when antigens and antibodies bind together.

IMMUNE DEFICIENCY: A breakdown or inability of certain parts of the immune system to function, thus making a person susceptible to certain diseases that they would not ordinarily develop.

IMMUNE RESPONSE: The activity of the immune system against foreign substances.

IMMUNE SYSTEM: The body's complicated natural defense against disruption caused by invading foreign agents (e.g., microbes, viruses). There are two aspects of the immune system's response to disease: innate and acquired. The innate part of the response is mobilized very quickly in response to infection and does not depend on recognizing specific proteins or antigens (see) foreign to an individual's normal tissue. It includes complement, macrophages, dendritic cells, and granulocytes. The acquired, or learned, immune response arises when dendritic cells and macrophages present pieces of antigen to lymphocytes, which are genetically programmed to recognize very specific amino acid sequences. The ultimate result is the creation of cloned (see clone) populations of antibody-producing B cells (see) and cytotoxic T lymphocytes (see) primed to respond to a unique pathogen.

IMMUNE THROMBOCYTOPENIC PURPURA (ITP): Also idiopathic immune thrombocytopenic purpura. A condition in which the body produces antibodies (see) against the platelets (see) in the blood, which are cells responsible for blood clotting. ITP is very common in persons infected with HIV.

IMMUNITY: A natural or acquired resistance to a specific disease. Immunity may be partial or complete, long lasting or temporary.

IMMUNIZATION: To protect against an infectious disease by vaccination (see), usually with a weakened (attenuated) or killed form of the disease-causing microorganism. While people are usually immunized against an infectious disease by getting vaccinated, having a disease such as measles, mumps, or rubella one time usually prevents or "immunizes" a person from getting this disease again.

IMMUNOCOMPETENT: 1. Capable of developing an immune response. 2. Possessing a normal immune system.

IMMUNOCOMPROMISED: Refers to an immune system in which the ability to resist or fight off infections and tumors is subnormal.

IMMUNODEFICIENCY: Breakdown in immunocompetence (see) when certain parts of the immune system no longer function. This condition makes a person more susceptible to certain diseases.

IMMUNOGEN: A substance, also called an antigen (see), capable of provoking an immune response (see).

IMMUNOGENICITY: The ability of an antigen (see) or vaccine to stimulate an immune response (see).

IMMUNOGLOBULIN (IG): (Ig) Also called immune serum globulin. A class of proteins also known as antibodies (see) made by the B cells (see) of the immune system (see) in response to a specific antigen (see), and containing a region that binds to this antigen (antigen-binding site). Each immunoglobulin is made up of two polypeptides (see), a heavy chain and a light chain. These heavy and light chains complex to

form the antigen binding site. Each group of immunoglobulins is named for the type of heavy chain that it contains. The heavy chain determines the post-antigen binding activity of an antibody. There are five classes of immunoglobulins: IgA, IgD, IgE, IgG, and IgM.

IMMUNOGLOBULIN A (IGA): (IgA) A class of antibodies (see), often formed as a dimer (i.e., two antibody molecules attached to each other end to end), that is secreted into bodily fluids such as saliva. IgA protects the body's mucosal surfaces from infections.

IMMUNOGLOBULIN D (IGD): (IgD) A class of antibodies (see) that is present in low concentration in serum (see). The primary function of IgD appears to be as an antigen (see) receptor on mature B cells (see).

IMMUNOGLOBULIN E (IGE): (IgE) A class of antibodies (see) involved in anti-parasite (see parasite) immunity and in allergies.

IMMUNOGLOBULIN G (IGG): (IgG) A class of antibodies (see) composed of two identical light and two identical heavy polypeptide chains. IgG acts on antigens by agglutinating (clumping cells together) them. In pregnancy, IgG crosses the placenta to the fetus and protects it against red cell antigens and white cell antigens. Also called gamma globulin (see).

IMMUNOGLOBULIN M (IGM): (IgM) A class of antibodies (see) that is made by the body as the initial response to an antigen (see). If IgM is made in response to a vaccination (see), a booster shot will result in a "switch" from IgM to mostly immunoglobulin G (see).

IMMUNOMODULATOR: Any substance that influences the immune system. See Interleukin–2; Immunostimulant; Immunosuppression.

IMMUNOSTIMULANT: Any agent or substance that triggers or enhances the body's defense; also called immunopotentiator.

IMMUNOSUPPRESSION: A state of the body in which the immune system (see) is damaged and does not perform its normal functions.

Immunosuppression may be induced by drugs (e.g., in chemotherapy) or result from certain disease processes, such as HIV infection.

IMMUNOTHERAPY: Treatment aimed at reconstituting an impaired immune system (see).

IMMUNOTOXIN: A plant or animal toxin (i.e., poison) that is attached to a monoclonal antibody (see) and used to destroy a specific target cell.

INCIDENCE: The number of new cases (e.g., of a disease) occurring in a given population over a certain period of time.

INCLUSION/EXCLUSION CRITERIA: The medical or social standards determining whether a person may or may not be allowed to enter a clinical trial. For example, some trials may not allow persons with chronic liver disease or with certain drug allergies; others may exclude men or women, or only include persons with a lowered T cell count.

INCUBATION PERIOD: The time interval between the initial infection with a pathogen (e.g., HIV) and the appearance of the first symptom or sign of disease.

IND: See Investigational New Drug.

INDIAN HEALTH SERVICE (IHS): An agency within the U.S. Department of Health and Human Services (see) responsible for providing federal health services to American Indians and Alaska Natives. The IHS currently provides health services to approximately 1.5 million American Indians and Alaska Natives who belong to more than 557 federally recognized tribes in 34 states. **Internet address: http://www.ihs.gov/.**

INDINAVIR: An FDA approved (03/14/96) protease inhibitor (see) for use alone or in combination with nucleoside analogs (see) for the treatment of HIV infection in adults. Also called Crixivan.

INFECTION: The state or condition in which the body (or part of the body) is invaded by an infectious agent (e.g., a bacterium, fungus, or virus), which multiplies and produces an injurious effect (active infection). As related to HIV: Infection typically begins when HIV encounters a CD4+ cell (see). The HIV surface protein gp120 (see) binds tightly to the CD4 molecule on the cell's surface. The membranes of the virus and the cell fuse, a process governed by gp41 (see), another surface protein. The viral core, containing HIV's RNA, proteins, and enzymes, is released into the cell.

INFECTIOUS: An infection capable of being transmitted by direct or intimate contact (e.g., sex).

INFORMED CONSENT: The permission granted by a participant in a research study (including medical research) after he/she has received comprehensive information about the study. This is a statement of trust between the institution performing the research procedure and the person (e.g., a patient) on whom the research procedures are to be performed. This includes, for example, the type of protection available to people considering entering a drug trial. Before entering the trial, participants must sign a consent form that contains an explanation of: (a) why the research is being done, (b) what the researchers want to accomplish, (c) what will be done during the trial and for how long, (d) what the risks associated with the trial are, (e) what benefits can be expected from the trial, (f) what other treatments are available, and (g) the participant's right to leave the trial at any time. Informed consent also pertains to situations where certain tests need to be performed. See Clinical Trial.

INFUSION: The process of administering therapeutic fluid, other than blood, to an individual by slowly injecting a dilute solution of the compound into a vein. Infusions are often used when the digestive system does not absorb appreciable quantities of a drug or when the drug is too toxic or the volume is too large to be given by quick injection.

INOCULATION: The introduction of a substance (inoculum; e.g., a vaccine, serum, or virus) into the body to produce or to increase immunity to the disease or condition associated with the substance. See Vaccine.

INSTITUTIONAL REVIEW BOARD (IRB): 1. A committee of physicians, statisticians, researchers, community advocates, and others that ensures that a clinical trial (see) is ethical and that the rights of study participants are protected. All clinical trials in the U.S. must be approved by an IRB before they begin. 2. Every institution that conducts or supports biomedical or behavioral research involving human subjects must, by federal regulation, have an IRB that initially approves and periodically reviews the research so as to protect the rights of human subjects.

INTEGRASE: A little-understood enzyme (see) that plays a vital role in the HIV-infection process. Integrase inserts HIV's genes into a cell's normal DNA (see). It operates after reverse transcriptase (see) has created a DNA version of the RNA (see) form of HIV genes present in virus particles. Substances that inhibit integrase are being studied in HIV-infected patients.

INTEGRASE INHIBITORS: A class of experimental anti-HIV drugs that prevents the HIV integrase (see) enzyme from inserting viral DNA into a host cell's normal DNA (see).

INTEGRATION: The process by which the different parts of an organism are made a functional and structural whole, especially through the activity of the nervous system and of hormones. As related to HIV: The process by which the viral DNA migrates to the cell's nucleus, where it is spliced into the host's DNA with the help of viral integrase (see). Once incorporated, HIV DNA is called the provirus and is duplicated together with the cell's genes every time the cell divides. Recent reports suggest that HIV's DNA also can integrate into the DNA of nondividing cells such as macrophages (see) and brain and nerve cells.

INTENT TO TREAT: Analysis of clinical trial (see) results that includes all data from patients in the groups to which they were randomized (i.e., assigned through random distribution) even if they never received the treatment.

INTERACTION: See Drug-Drug Interaction.

INTERFERON: One of a number of antiviral proteins that modulate the immune response. Interferon alpha (IFNa) is secreted by a virally infected cell and strengthens the defenses of nearby uninfected cells. A manufactured version of IFNa (trade names: Roferon, Intron A) is an FDA-approved treatment for Kaposi's Sarcoma (see), hepatitis B virus, and hepatitis C virus. Interferon gamma is synthesized by immune system cells (Natural Killer [NK] Cells and CD4 cells; see). It activates macrophages (see) and helps orient the immune system to a mode that promotes cellular immunity (Thl response; see).

INTERLEUKINS: One of a large group of glycoproteins that act as cytokines (see). The interleukins are secreted by and affect many different cells in the immune system. See Biotechnology; B Lymphocytes; Genetic Engineering; Killer T Cells; Natural Killer Cells (NK); Lymphocyte; T Cells.

INTERLEUKIN-1 (IL-1): A cytokine (see) that is released early in an immune system response by monocytes and macrophages. It stimulates T cell proliferation and protein synthesis. Another effect of IL–1 is that it causes fever.

INTERLEUKIN-2 (IL-2): A cytokine (see) secreted by Th1 (see) CD4 cells to stimulate CD8 cytotoxic T lymphocytes (see). IL–2 also increases the proliferation and maturation of the CD4 cells themselves. During HIV infection, IL-2 production gradually declines. Commercially, IL–2 is produced by recombinant DNA technology and is approved by the FDA for the treatment of metastatic renal (i.e., kidney) cell cancer. Recent data suggest that therapy with subcutaneous IL–2,

in combination with antiretroviral drugs (see), has the potential to halt the usual progression of HIV disease by maintaining an individual's CD4+ T cell count in the normal range for prolonged periods of time.

INTERLEUKIN-4 (IL-4): A cytokine (see) secreted by Th2 (see) CD4 cells that promotes antibody production by stimulating B cells to proliferate and mature.

INTERLEUKIN-12 (IL-12): A cytokine released by macrophage (see) in response to infection that promotes the activation of cell-mediated immunity. Specifically, IL-12 triggers the maturation of Thl (see) CD4 cells, specific cytotoxic T lymphocyte responses, and an increase in the activity of NK cells (see). IL-12 is under study as an immunotherapy (see) in HIV infection.

INTERSTITIAL: Relating to or situated in the small, narrow spaces between tissues or parts of an organ.

INTRAMUSCULAR (IM): Injected directly into a muscle.

INTRATHECAL: Injected into the fluid surrounding the spinal cord.

INTRAVENOUS (IV): Of or pertaining to the inside of a vein, as of a thrombus. An injection made directly into a vein.

INTRAVENOUS IMMUNOGLOBULIN (IVIG): A sterile solution of concentrated antibodies extracted from healthy people. IVIG is used to prevent bacterial infections in persons with low or abnormal antibody production. Injected into a vein.

INTRAVITREAL: Within the eye.

INVESTIGATIONAL NEW DRUG (IND): The status of an experimental drug after the FDA agrees that it can be tested in people.

INVIRASE: See Saquinavir.

IN VITRO: ("In glass.") An artificial environment created outside a living organism (e.g., a test tube or culture plate) used in experimental research to study a disease or process.

IN VIVO: ("In life.") Studies conducted within living organisms (e.g., animal or human studies).

IRB: See Institutional Review Board.

ISOLATE: An individual (as a spore or a single organism), viable part of an organism (as a cell), or a strain that has been separated (as from diseased tissue, contaminated water, or the air) from the whole. Also, a pure culture produced from such an isolate. A particular strain of HIV taken from a patient.

ITP: See Immune Thrombocytopenic Purpura.

IVIG: See Intravenous Immune Globulin.

JAUNDICE: Yellow pigmentation of the skin and whites of the eyes caused by elevated blood levels of bilirubin (see). The condition is associated with either liver or gallbladder disease or excessive destruction of red blood cells.

JC VIRUS: See PML; Papilloma.

KAPOSI'S SARCOMA (KS): An AIDS-defining illness consisting of individual cancerous lesions caused by an overgrowth of blood vessels. KS typically appears as pink or purple painless spots or nodules on the surface of the skin or oral cavity. KS also can occur internally, especially in the intestines, lymph nodes, and lungs, and in this case is life threatening. The cancer may spread and also attack the eyes. There has been considerable speculation that KS is not a spontaneous cancer but is sparked by a virus. A species of herpes virus—also referred to as Kaposi's Sarcoma herpes virus (KSHV) or HHV–8—similar to the Epstein–Barr virus (see) is currently under extensive investigation. Up to now, KS has been treated with alpha interferon (see), radiation therapy (outside the oral cavity), and various systemic and intralesional cancer chemotherapies.

KARNOFSKY SCORE: A score between 0 and 100 assigned by a clinician based on observations of a patient's ability to perform common tasks. Thus, 100 signifies normal physical abilities with no evidence of disease. Decreasing numbers indicate a reduced ability to perform activities of daily living.

KILLER T CELLS: Because viruses lurk inside host (e.g., human) cells where antibodies cannot reach them, the only way they can be eliminated is by killing the infected host cell. To do this, the immune system uses a kind of white blood cell, called killer T cells. These cells act only when they encounter another cell that carries a "marker" (i.e., a protein) that links it to a foreign protein—that of the invading virus. Killer T cells can themselves become infected by HIV or other viruses, or transformed by cancer. Also known as cytotoxic T cells (or cytotoxic T lymphocytes). See NK (natural killer) Cells; Null Cell; T Cells.

KSHV: Kaposi's Sarcoma Herpes Virus. See Kaposi's Sarcoma.

KUPFFER CELLS: Specialized macrophages in the liver. See Macrophage.

LAI: A group of closely related HIV isolates (see) that includes the LAV, IIIB, and BRU strains of HIV. Used in HIV vaccine development.

LAK CELLS: Lymphocytes (see) transformed in the laboratory into lymphokine (see) activated killer cells, which attack tumor cells.

LAMIVUDINE: A nucleoside reverse transcriptase inhibitor (see) first approved by FDA in 1995 and used in combination with other antiretroviral agents (see) for adults, adolescents, and children. Also called 3TC or Epivir and available with Zidovudine (see) as Combivir (see).

LANGERHANS CELLS: Dendritic cells (see) in the skin that pick up an antigen (see) and transport it to the lymph nodes (see).

LAS: See Lymphadenopathy Syndrome.

LATENCY: The period when an infecting organism is in the body but is not producing any clinically noticeable ill effects or symptoms. In HIV disease, clinical latency is an asymptomatic period in the early years of HIV infection. The period of latency is characterized in the peripheral blood by near normal CD4 (see) counts. Recent research indicates that HIV remains quite active in the lymph nodes during this period. Cellular latency is the period after HIV has integrated its genome (see) into a cell's DNA (see) but has not yet begun to replicate.

LD50: Short for "Lethal Dose 50." In toxicology, the amount of a substance sufficient to kill one-half of the population of test subjects (e.g., mice or rats).

LENTIVIRUS: "Slow" virus characterized by a long interval between infection and the onset of symptoms. HIV is a lentivirus as is the simian immunodeficiency virus (SIV) (see) that infects non-human primates.

LESION: A general term to describe an area of altered tissue (e.g., the infected patch or sore in a skin disease).

LEUKOCYTES: Any of the various white blood cells that together make up the immune system. Neutrophils, lymphocytes, and monocytes are all leukocytes.

LEUKOCYTOSIS: An abnormally high number of leukocytes in the blood. This condition can occur during many types of infection and inflammation.

LEUKOPENIA: A decrease in the number of white blood cells. The threshold value for leukopenia is usually taken as less than 5,000 white blood cells per cubic millimeter of blood.

LEUKOPLAKIA: See Oral Hairy Leukoplakia.

LIP: See Lymphoid Interstitial Pneumonitis.

LIPID: Any of a group of fats and fatlike compounds, including sterols, fatty acids, and many other substances.

LIPODYSTROPHY: A disturbance in the way the body produces, uses, and distributes fat. Lipodystrophy is also referred to as "buffalo hump," "protease paunch," or "Crixivan potbelly." In HIV disease, lipodystrophy has come to refer to a group of symptoms that seem to be related to the use of protease inhibitor (see) drugs. How protease inhibitors may cause or trigger lipodystrophy is not yet known. Lipodystrophy symptoms involve the loss of the thin layer of fat under the skin, making veins seem to protrude; wasting of the face and limbs; and the accumulation of fat on the abdomen (both under the skin and within the abdominal cavity) or between the shoulder blades. Women may also experience narrowing of the hips and enlargement of the breasts.

LIPOSOMES: A spherical particle in an aqueous (watery) medium (e.g., inside a cell) formed by a lipid (see) bilayer enclosing an aqueous compartment. Microscopic globules of lipids are manufactured to

enclose medications. The fatty layer of the liposome is supposed to protect and confine the enclosed drug until the liposome binds with the outer membrane of target cells. By delivering treatments directly to the cells needing them, drug efficacy may be increased while overall toxicity is reduced.

LIVE VECTOR VACCINE: As pertaining to HIV, a vaccine that uses an attenuated (i.e., weakened) virus or bacterium to carry pieces of HIV into the body to directly stimulate a cell-mediated immune response.

LIVER FUNCTION TEST: A test that measures the blood serum level of any of several enzymes (e.g., SGOT and SGPT; see) produced by the liver. An elevated liver function test is a sign of possible liver damage.

LOG: Changes in viral load are often reported as logarithmic or "log changes." This mathematical term denotes a change in value of what is being measured by a factor of 10. For example, if the baseline viral load by PCR were 20,000 copies/ml plasma, then a 1-log increase equals a 10-fold (10 times) increase or 200,000 copies/ml plasma. A 2-log increase equals 2,000,000 copies/ml plasma, or a 100-fold increase.

LONG TERMINAL REPEAT SEQUENCE (LTR): The genetic material at each end of the HIV genome (see). When the HIV genome is integrated into a cell's own genome, the LTR interacts with cellular and viral factors to trigger the transcription of the HIV-integrated HIV DNA (see) genes into an RNA (see) form that is packaged in new virus particles. Activation of LTR is a major step in triggering HIV replication.

LONG-TERM NONPROGRESSORS: Individuals who have been living with HIV for at least 7 to 12 years (different authors use different time spans) and have stable CD4+ T cell counts of 600 or more cells per cubic millimeter of blood, no HIV-related diseases, and no previous antiretroviral therapy. Data suggest that this phenomenon is associated with the maintenance of the integrity of the lymphoid tissues and with less virus trapping in the lymph nodes than is seen in other individuals living with HIV.

LTR: See Long Terminal Repeat Sequence.

LUMBAR: Lower back region. Of, relating to, or constituting the vertebrae between the thoracic vertebrae and the sacrum region. The sacrum is the triangular bone made up of five fused vertebrae and forming the posterior section of the pelvis. The thorax is the part of the human body between the neck and the diaphragm, partially encased by the ribs and containing the heart and lungs (i.e., the chest).

LUMBAR PUNCTURE: A procedure in which cerebrospinal fluid from the subarachnoid space (see) in the lumbar (see) region is tapped for examination. Also known as spinal tap.

LYMPH: A transparent, slightly yellow fluid that carries lymphocytes (see). Lymph is derived from tissue fluids collected from all parts of the body and is returned to the blood via lymphatic vessels (see).

LYMPH NODES: Small, bean-sized organs of the immune system, distributed widely throughout the body. Lymph fluid is filtered through the lymph nodes in which all types of lymphocytes (see) take up temporary residence. Antigens (see) that enter the body find their way into lymph or blood and are filtered out by the lymph nodes or spleen, respectively, for attack by the immune system.

LYMPHADENOPATHY SYNDROME (LAS): Swollen, firm, and possibly tender lymph nodes (see). The cause may range from an infection such as HIV, the flu, or mononucleosis to lymphoma (cancer of the lymph nodes).

LYMPHATIC VESSELS: A body-wide network of channels, similar to the blood vessels, that transport lymph (see) to the immune organs and into the bloodstream.

LYMPHOCYTE: A white blood cell. Present in the blood, lymph (see), and lymphoid tissue. See B Lymphocytes; T Cells.

LYMPHOID INTERSTITIAL PNEUMONITIS (LIP): A type of pneumonia that affects 35 to 40 percent of children with AIDS, which causes hardening of the lung membranes involved in absorbing oxygen. LIP is an AIDS-defining illness in children. The etiology (cause) of LIP is not clear. There is no established therapy for LIP, but the use of corticosteroids for progressive LIP has been advocated.

LYMPHOID ORGANS: Include tonsils, adenoids, lymph nodes (see), spleen, thymus, and other tissues. These organs act as the body's filtering system, trapping invaders (i.e., foreign particles, e.g., bacteria and viruses) and presenting them to squadrons of immune cells that congregate there. Within these lymphoid tissues, immune activity is concentrated in regions called germinal centers, where the thread-like tentacles of follicular dendritic cells (FDCs) (see) form networks that trap invaders.

LYMPHOID TISSUE: See Lymphoid Organs.

LYMPHOKINES: 1. Products of the lymphatic cells that stimulate the production of disease-fighting agents and the activities of other lymphatic cells. Among the lymphokines are gamma interferon (see) and interleukin–2 (see). 2. Non-antibody mediators of immune responses (see), released by activated lymphocytes (see).

LYMPHOMA: Cancer of the lymphoid tissues. Lymphomas are often described as being "large cell" or "small cell" types, cleaved or non-cleaved, or diffuse or nodular. The different types often have different prognoses (i.e., prospect of survival or recovery). Some of these lymphomas are named after the physicians who first described them (e.g., Burkitt's lymphoma, Hodgkin's disease). Lymphomas can also be referred to by the organs where they are active such as CNS lymphomas, which are in the central nervous system, and GI lymphomas, which are in the gastrointestinal tract. The types of lymphomas most commonly associated with HIV infection are called non-Hodgkin's lympho-

mas or B cell lymphomas. In these types of cancers, certain cells of the lymphatic system grow abnormally. They divide rapidly, growing into tumors.

LYMPHOPENIA: A relative or absolute reduction in the number of lymphocytes (see) in the circulating blood.

LYMPHOPROLIFERATIVE RESPONSE: A specific immune response that entails rapid T cell (see) replication. Standard antigens, such as tetanus toxoid, that elicit this response, are used in lab tests of immunocompetency (see).

LYSIS: Rupture and destruction of a cell.

MAC: See Mycobacterium Avium Complex.

MACROPHAGE: A large immune cell that devours invading pathogens and other intruders. Stimulates other immune cells by presenting them with small pieces of the invader. Macrophages can harbor large quantities of HIV without being killed, acting as reservoirs of the virus.

MACROPHAGE-TROPIC VIRUS: HIV strains that preferentially infect macrophages (see) in cell culture experiments. They readily fuse with cells that have both CD4 (see) and CCR5 (see) molecules on their surfaces, whereas the same viral isolates fail to fuse with cells expressing only CD4. These isolates are the main strains found in patients during the symptom-free stage of HIV disease.

MAGNETIC RESONANCE IMAGING (MRI): A noninvasive, non-x-ray diagnostic technique—also called nuclear magnetic resonance or NMR—based on the magnetic fields of hydrogen atoms in the body. MRI provides computer-generated images of the body's internal tissues and organs.

MAI: See Mycobacterium Avium Complex.

MAJOR HISTOCOMPATIBILITY COMPLEX (MHC): Two classes of molecules on cell surfaces. MHC class I molecules exist on all cells, and hold and present foreign antigens (see) to CD8 cytotoxic T lymphocytes (see) if the cell is infected by a virus or other microbe. MHC class II molecules are the billboards of the immune system. Peptides derived from foreign proteins are inserted into MHC's binding groove and displayed on the surface of antigen-presenting cells. These peptides are then recognized by T lymphocytes so that the immune system is alerted to the presence of foreign material. See Histocompatibility Testing.

MALABSORPTION SYNDROME: Decreased intestinal absorption resulting in loss of appetite, muscle pain, and weight loss. See AIDS Wasting Syndrome.

MALAISE: A generalized, nonspecific feeling of discomfort.

MALIGNANT: Refers to cells or tumors growing in an uncontrolled fashion. Such growths may spread to and disrupt nearby normal tissue, or reach distant sites via the bloodstream. By definition, cancers are always malignant, and the term "malignancy" implies cancer. See Metastasis.

MAST CELL: A granulocyte (see) found in tissue. The contents of the mast cells, along with those of basophils (see), are responsible for the symptoms of allergy.

MEMORY T CELLS: A subset of T lymphocytes (see) that have been exposed to specific antigens (see) and can then proliferate (i.e., reproduce) on subsequent immune system encounters with the same antigen.

MENINGES: Membranes surrounding the brain or spinal cord. Part of the so-called "blood-brain barrier." See Meningitis.

MENINGITIS: An inflammation of the meninges (membranes surrounding the brain or spinal cord), which may be caused by a bacterium, fungus, or virus. See Cryptococcal Meningitis; Central Nervous System.

MESSENGER RNA: Also referred to as mRNA. An RNA (ribonucleic acid; see) that carries the genetic code for a particular protein from the DNA in the cell's nucleus to a ribosome (see) in the cytoplasm (see) and acts as a template, or pattern, for the formation of that protein.

METABOLISM: The sum of the processes by which a particular substance is handled (as by assimilation and incorporation, or by detoxification and excretion) in the living body.

METABOLITE: Any substance produced by metabolism (see) or by a metabolic process.

METASTASIS: Transfer of a disease-producing agent (e.g., cancer cells or bacteria) from an original site of disease to another part of the body, with development of a similar lesion in the new location (e.g., spread of cancer from an original site to other sites in the body).

MHC: See Major Histocompatibility Complex.

MICROBES: Microscopic living organisms, including bacteria, protozoa, viruses, and fungi.

MICROBICIDE: An agent (e.g., a chemical or antibiotic) that destroys microbes (see). New research is being carried out to evaluate the use of rectal and vaginal microbicides to inhibit the transmission of sexually transmitted diseases, including HIV.

MICROENCAPSULATED: Surrounded by a thin layer of protection. A means of protecting a drug or vaccine from rapid breakdown.

MICROSPORIDIOSIS: An intestinal infection that causes diarrhea (see) and wasting in persons with HIV. It results from two different species of microsporidia, a protozoal parasite. See Pathogen; Protozoa; AIDS Wasting Syndrome.

MITOCHONDRIA: Organelles (particles of a living substance) within the cytoplasm (see) of the cells, mitochondria have their own independent DNA, and serve as a source of energy for the cell.

MN: A strain of HIV used in vaccine development.

MOLECULE: The smallest particle of a compound that has all the chemical properties of that compound. Molecules are made up of two or more atoms, either of the same element or of two or more different elements. Ionic compounds, such as common salt, are made up not of molecules, but of ions arranged in a crystalline structure. Unlike ions, molecules carry no electrical charge. Molecules differ in size and molecular weight as well as in structure.

MOLLUSCUM CONTAGIOSUM: A disease of the skin and mucous membranes caused by a poxvirus (molluscum contagiosum virus, MCV) infection. It is characterized by small dome-shaped papules (bumps) on the face, upper trunk, or extremities. The disease most frequently occurs in children and adults with impaired immune response. It is transmitted from person to person by direct contact. It is also autoinoculable (i.e., a secondary infection produced by contact with a lesion on one's own body). In persons living with HIV, molluscum contagiosum is often a progressive disease, resistant to treatment. When CD4+ cells fall below 200, the lesions tend to proliferate and spread.

MONOCLONAL ANTIBODIES: Antibodies (see) produced in the laboratory by a hybridoma (see) or antibody-producing cell source for a specific antigen (see). Monoclonal antibodies are useful as tools for identifying specific protein molecules.

MONOCYTE: A large white blood cell that ingests microbes or other cells and foreign particles. When a monocyte enters tissues, it develops into a macrophage (see).

MONONEURITIS MULTIPLEX (MM): A rare type of neuropathy (see) that has been described with HIV infection. It may fall into two different settings. One type occurs during the early period of the infection and has a more benign outcome. The second form occurs later and is more aggressive, leading to progressive paralysis and death in some patients. It has been suggested that MM is related to multifocal cytomegalovirus (CMV) (see) infection.

MONOVALENT VACCINE: A vaccine that is specific for only one antigen (see).

MORBIDITY: The condition of being diseased or sick; also the incidence of disease or rate of sickness.

MRI: See Magnetic Resonance Imaging.

MUCOCUTANEOUS: Anything that concerns or pertains to mucous membranes (see) and the skin (e.g., mouth, eyes, vagina, lips, or anal area).

MUCOSA: See Mucous Membrane.

MUCOSAL IMMUNITY: Resistance to infection across the mucous membranes (see). Dependent on immune cells and antibodies (see) present in the lining of the urogenital tract, gastrointestinal tract, and other parts of the body exposed to the outside world.

MUCOUS MEMBRANE: Moist layer of tissue lining the digestive, respiratory, urinary, and reproductive tracts—all the body cavities with openings to the outside world except the ears.

MULTIPLE DRUG RESISTANT TUBERCULOSIS (MDR-TB): A strain of TB (see tuberculosis) that does not respond to two or more standard anti-TB drugs. MDR–TB usually occurs when treatment is interrupted, thus allowing organisms, in which mutations for drug resistance have occurred, to proliferate.

MUTATION: In biology, a sudden change in a gene or unit of hereditary material that results in a new inheritable characteristic. In higher animals and many higher plants, a mutation may be transmitted to future generations only if it occurs in germ—or sex cell—tissue; body cell mutations cannot be inherited. Changes within the chemical structure of single genes (see) may be induced by exposure to radiation, temperature extremes, and certain chemicals. The term mutation may also be used to include losses or rearrangements of segments of chromosomes, the long strands of genes. Mutation, which can establish new traits in a population, is important in evolution. As related to HIV: During the course of HIV disease, HIV strains may emerge in an infected individual that differ widely in their ability to infect and kill different cell types, as well as in their rate of replication. Of course, HIV does not mutate into another type of virus.

MYALGIA: Diffuse muscle pain, usually accompanied by malaise (vague feeling of discomfort or weakness).

MYCOBACTERIUM: Any bacterium of the genus *Mycobacterium* or a closely related genus.

MYCOBACTERIUM AVIUM COMPLEX (MAC): 1. A common opportunistic infection (see) caused by two very similar mycobacterial organisms, *Mycobacterium avium* and *Mycobacterium intracellulare (MAI),* found in soil and dust particles. 2. A bacterial infection that can be localized (limited to a specific organ or area of the body) or disseminated throughout the body. It is a life-threatening disease, although new therapies offer promise for both prevention and treatment. MAC disease is extremely rare in persons who are not infected with HIV.

MYCOPLASMA: 1. Smallest free-living organisms known to infect humans. Mycoplasma cause a variety of illnesses, especially of the lungs and sexual organs. 2. Any microorganism of the genus *Mycoplasma,* also called pleuropneumonia-like organism.

MYCOSIS: Any disease caused by a fungus (see).

MYELIN: A substance that sheathes nerve cells, acting as an electric insulator that facilitates the conduction of nerve impulses. See Chronic Idiopathic Demyelinating Polyneuropathy.

MYELOPATHY: Any disease of the spinal cord.

MYELOSUPPRESSION: Suppression of bone marrow activity, causing decreased production of red blood cells (anemia), white blood cells (leukopenia; see), or platelets (thrombocytopenia; see). Myelosuppression is an effect of some drugs, such as AZT (see).

MYELOTOXIC: Destructive to bone marrow.

MYOCARDIAL: Refers to the heart's muscle mass.

MYOPATHY: Progressive muscle weakness. Myopathy may arise as a toxic reaction to AZT (see) or as a consequence of the HIV infection itself.

NADIR: The lowest point, such as the blood count after it has been depressed by chemotherapy. When applied to drugs, the lowest concentration of a drug in the body.

NATIONAL AIDS HOTLINE: See CDC National AIDS Hotline.

NATIONAL CANCER INSTITUTE (NCI): An institute of the National Institutes of Health (NIH) (see) with the overall mission of conducting and supporting research, training, and disseminating health information with respect to the causes, diagnosis, and treatment of cancer. NCI also performs these functions for HIV-related cancers. **Internet address: http://www.nci.nih.gov/.**

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES (NIAID): An NIH (see) institute that conducts and supports research to study the causes of allergic, immunologic, and infectious diseases, and to develop better means of preventing, diagnosing, and treating illnesses. NIAID is responsible for the federally funded, national basic research program in AIDS. It supports basic research, epidemiology, and natural history studies; blood screening tests; drug discovery and development; vaccine development and testing; and treatment studies, some directly and some through contracts and cooperative agreements with other institutions. It administers the Adult AIDS Clinical Trials Group (AACTG) (see) and the Pediatric AIDS Clinical Trials Group (see), network of testing units at hospitals around the country. NIAID also administers the Community Programs for Clinical Research on AIDS (CPCRA) (see) a community-based network of AIDS treatment research centers. **Internet address: http://www.niaid.nih.gov/.**

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT (NICHD): An NIH (see) institute that conducts and

supports research on the reproductive, developmental, and behavioral processes that determine the health of children, adults, families, and populations. Thus, NICHD supports clinical research related to the transmission of HIV from infected mothers to their offspring, the progression of disease in HIV-infected infants and children, and the testing of potential therapies and preventatives for this population. **Internet address: http://www.nih.gov/nichd/.**

NATIONAL INSTITUTES OF HEALTH (NIH): A multi-institute agency of the U.S. Department of Health and Human Services (see), NIH is the federal focal point for health research. It conducts research in its own laboratories and supports research in universities, medical schools, hospitals, and research institutions throughout this country and abroad. **Internet address: http://www.nih.gov/.**

NATIONAL LIBRARY OF MEDICINE (NLM): An NIH (see) institute, NLM is one of three U.S. national libraries. It is the world's largest research library in a single scientific and professional field (i.e., medicine). In the HIV/AIDS area, NLM provides electronic and print information services including the online services AIDSLINE, AIDSTRIALS, and AIDSDRUGS. (See entries for these services). **Internet address: http://www.nlm.nih.gov/.**

NATIONAL PREVENTION INFORMATION NETWORK (NPIN): See CDC National Prevention Information Network.

NATURAL HISTORY STUDY: Study of the natural development of something (such as an organism or a disease) over a period of time.

NATURAL KILLER CELLS (NK CELLS): A type of lymphocyte (see). Like cytotoxic T cells, NK cells attack and kill tumor cells and protect against a wide variety of infectious microbes. They are "natural" killers because they do not need additional stimulation or need to recognize a specific antigen in order to attack and kill. Persons with immunodeficiencies such as those caused by HIV infection have a decrease in "natural" killer cell activity. See Antigen; B Lymphocytes; T Cells; Null Cell.

NCI: See National Cancer Institute.

NDA: See New Drug Application.

NEBULIZED: See Aerosolized.

NECROLYSIS: Shedding of surface components of tissue, such as cells from internal body surfaces, due to death of a portion of tissue.

NEF: *(nef)* One of the regulatory genes of HIV. Three HIV regulatory genes—*tat, rev,* and *nef*— and three so-called auxiliary genes—*vif, vpr,* and *vpu*—contain information necessary for the production of proteins that control the virus' ability to infect a cell, produce new copies of itself, or cause disease. See *rev*; *tat*.

NELFINAVIR: An FDA approved (03/14/97) protease inhibitor (see) for the treatment of HIV infection when antiretroviral therapy is warranted in adults and children 2 years of age and older. Also called Viracept.

NEONATAL: Concerning the first 4 weeks of life after birth.

NEOPLASM: An abnormal and uncontrolled growth of tissue; a tumor.

NEPHROTOXIC: Poisonous to the kidneys.

NEURALGIA: A sharp, shooting pain along a nerve pathway.

NEUROLOGICAL COMPLICATIONS OF AIDS: See Central Nervous System (CNS) Damage.

NEUROPATHY: The name given to a group of disorders involving nerves. Symptoms range from a tingling sensation or numbness in the toes and fingers to paralysis. It is estimated that 35 percent of persons with HIV disease have some form of neuropathy. See Peripheral Neuropathy.

NEUTRALIZATION: The process by which an antibody (see) binds to specific antigens (see), thereby "neutralizing" the microorganism.

NEUTRALIZING ANTIBODY: An antibody (see) that keeps a virus from infecting a cell, usually by blocking receptors (see) on the cell or the virus.

NEUTRALIZING DOMAIN: The section of the HIV envelope protein, gp120 (see), that elicits antibodies with neutralizing activities.

NEUTROPENIA: An abnormal decrease in the number of neutrophils (the most common type of white blood cells) in the blood. The decrease may be relative or absolute. Neutropenia may also be associated with HIV infection or may be drug induced.

NEUTROPHIL: Also called polymorphonuclear neutrophil (PMN) leukocyte. A white blood cell that plays a central role in defense of a host against infection. Neutrophils engulf and kill foreign microorganisms.

NEVIRAPINE: A non-nucleoside reverse transcriptase inhibitor (see) first approved by FDA in 1996 and used in combination with antiretroviral agents (see) for the treatment of HIV–1 infection in adults and children 2 months of age or older. Also called Viramune.

NEW DRUG APPLICATION (NDA): An application submitted by the manufacturer of a drug to the FDA—after clinical trials have been completed—for a license to market the drug for a specified indication.

NIAID: See National Institute of Allergy and Infectious Diseases.

NICHD: See National Institute of Child Health and Human Development.

NIGHT SWEATS: Extreme sweating during sleep. Although they can occur with other conditions, night sweats are also a symptom of HIV disease.

NIH: See National Institutes of Health.

NK CELL: See Natural Killer Cells.

NLM: See National Library of Medicine.

NNRTI: See Non-Nucleoside Reverse Transcriptase Inhibitors.

NON-HODGKIN'S LYMPHOMA (NHL): A lymphoma (see) made up of B cells and characterized by nodular or diffuse tumors that may appear in the stomach, liver, brain, and bone marrow of persons with HIV. After Kaposi's Sarcoma (see), NHL is the most common opportunistic cancer in persons with AIDS.

NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTI): A group of structurally diverse compounds that bind to the catalytic site of HIV–1's reverse transcriptase (see). They are quite specific; unlike the nucleoside reverse transcriptase inhibitors (see), the NNRTIs have no activity against HIV–2 (see). As noncompetitive inhibitors of reverse transcriptase, their antiviral activity is additive or synergistic with most other antiretroviral agents (see). However drug-drug interactions (see) may dictate dosage adjustments with protease inhibitors (see). FDA has approved the NNRTIs nevirapine (see), delavirdine (see), and efavirenz (see) for use against HIV.

NORVIR: See Ritonavir.

NSAID: Nonsteroidal anti-inflammatory (reduces inflammation) drug.

NUCLEIC ACID: Organic substance, found in all living cells, in which the hereditary information is stored and from which it can be transferred. Nucleic acid molecules are long chains that generally occur in combination with proteins. The two chief types are DNA (deoxyribonucleic acid), found mainly in cell nuclei, and RNA (ribonucleic acid), found mostly in cytoplasm. See Gene; Genetic Engineering; Mutation.

NUCLEOCAPSID: The viral genome (see) is surrounded by a protein coating or shell called the capsid. The genome plus the capsid is called the nucleocapsid.

NUCLEOLI: Bodies in the nucleus that become enlarged during protein synthesis and contain the DNA template for ribosomal RNA. See Ribonucleic Acid; Ribosome.

NUCLEOSIDE: A building block of nucleic acids (see), DNA (see), or RNA (see), the genetic material found in living organisms. Nucleosides are nucleotides (see) without the phosphate groups.

NUCLEOSIDE ANALOG: An artificial copy of a nucleoside (see). When incorporated into a virus' DNA (see) or RNA (see) during viral replication, the nucleoside analog acts to prevent production of new virus. Nucleoside analogs may take the place of natural nucleosides, blocking the completion of a viral DNA chain during infection of a new cell by HIV. The HIV enzyme reverse transcriptase (see) is more likely to incorporate the nucleoside analogs into the DNA it is constructing than is the DNA polymerase (see) normally used for DNA creation in cell nuclei. There are currently seven (or six without combivir) antiretroviral nucleoside analogs approved for marketing in the United States: AZT, ddI, ddC, d4T, 3TC, combivir, and abacavir (see entries for these terms).

NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR (NRTI): A nucleoside analog (see) antiretroviral drug whose chemical structure constitutes a modified version of a natural nucleoside (see). These compounds suppress replication of retroviruses (see) by interfering with the reverse transcriptase (see) enzyme. The nucleoside analogs cause premature termination of the proviral (viral precursor) DNA (see) chain. All NRTIs require phosphorylation in the host's cells prior to their incorporation into the viral DNA. The class of anti-HIV NRTIs includes such drugs as AZT, ddI, ddC, d4T, 3TC, and abacavir.

NUCLEOTIDE: Nucleotides are the building blocks of nucleic acids (see), DNA (see), and RNA (see). Nucleotides are composed of phosphate groups, a five-sided sugar molecule (ribose sugars in RNA,

deoxyribose sugars in DNA), and nitrogen containing bases. These fall into two classes: pyrimidines and purines. A nucleotide without its phosphate group is called a nucleoside.

NUCLEOTIDE ANALOGS: Nucleotide analogs are drugs that are structurally related to nucleotides (see); they are chemically altered to inhibit production or activity of disease-causing proteins. The chemical structures of these drugs may cause them to replace natural nucleotides in the viral DNA nucleic acid (see) sequence. Nucleotide analogs do not require as much phosphorylation in the host's cells as the nucleoside reverse transcriptase inhibitors (see) to become active drugs. The nucleotide analog cidofovir (also known as HPMC) is approved for CMV retinitis. Adefovir is under investigation for HIV and HBV.

NUCLEUS: 1. The central controlling body within a living cell, usually a spherical unit enclosed in a membrane and containing genetic codes for maintaining the life systems of the organism and for issuing commands for growth and reproduction. 2. The nucleus of a cell is essential to such cell functions as reproduction and protein synthesis. It is composed of nuclear sap and a nucleoprotein-rich network from which chromosomes and nucleoli (see) arise, and is enclosed in a definite membrane.

NULL CELL: A lymphocyte (see) that develops in the bone marrow and lacks the characteristic surface markers of the B and T lymphocytes. Null cells represent a small proportion of the lymphocyte population. Stimulated by the presence of antibody, null cells can attack certain cellular targets directly and are known as "natural killer" or NK cells (see).

OCULAR: Pertaining to the eye.

OFFICE OF AIDS RESEARCH (OAR): An office within the National Institutes of Health (NIH) (see) that coordinates AIDS research in all of the participating NIH institutes. **Internet address: http://www.nih.gov/od/oar/index.htm/.**

OFF-LABEL USE: A drug prescribed for conditions other than those approved by the FDA.

ONCOLOGY: Study of cancers or other tumors.

OPEN-LABEL TRIAL: A clinical trial (see) in which doctors and participants know which drug or vaccine is being administered.

OPPORTUNISTIC INFECTIONS: Illnesses caused by various organisms, some of which usually do not cause disease in persons with normal immune systems. Persons living with advanced HIV infection suffer opportunistic infections of the lungs, brain, eyes, and other organs. Opportunistic infections common in persons diagnosed with AIDS include Pneumocystis carinii pneumonia (see); Kaposi's Sarcoma (see); cryptosporidiosis (see); histoplasmosis (see); other parasitic, viral, and fungal infections; and some types of cancers.

ORAL HAIRY LEUKOPLAKIA (OHL): A whitish lesion that appears on the side of the tongue and inside cheeks. The lesion appears raised, with a ribbed or "hairy" surface. OHL occurs mainly in persons with declining immunity and may be caused by Epstein–Barr virus (see) infection. OHL was not observed before the HIV epidemic.

ORGANELLE: Any one of various particles of living substance bound within most cells, such as the mitochondria, the Golgi complex, the endoplastic reticulum, the lysosomes, and the centrioles.

OROPHARYNGEAL: Relating to that division of the pharynx between the soft palate and the epiglottis. Pharynx is a tube that connects the mouth and nasal passages with the esophagus, the connection to the stomach. Epiglottis is a thin, valvelike structure that covers the glottis, the opening of the upper part of the larynx (the part of the throat containing the vocal cords), during swallowing.

ORPHAN DRUGS: An FDA (see) category that refers to medications used to treat diseases and conditions that occur rarely. Therefore, there is little financial incentive for the pharmaceutical industry to develop such medications. Orphan drug status gives a manufacturer specific financial incentives to develop and provide such medications.

P24: (p24) A bullet-shaped core made of another protein that surrounds the viral RNA (see) within the envelope of HIV. The p24 antigen test looks for the presence of this protein in a patient's blood. A positive result for the p24 antigen suggests active HIV replication. p24 found in the peripheral blood is also thought to correlate with the amount of virus in the peripheral blood. Measurement of p24 levels in the blood has been used to monitor viral activity, although this is not considered a very accurate method due to the existence of the p24 antibody that binds with the antigen and makes it undetectable. See Branched DNA Assay.

PACKAGE INSERT: A document, approved by the FDA and furnished by the manufacturer of a drug, for use when dispensing the drug (i.e., inserted into the package). The document indicates approved uses, contraindications, and potential side effects.

PALLIATIVE: A treatment that provides symptomatic relief but not a cure.

PALLIATIVE CARE: Palliative care is an approach to life-threatening chronic illnesses, especially at the end of life. Palliative care combines active and compassionate therapies to comfort and support patients and their families who are living with life-ending illness. Palliative care strives to meet physical needs through pain relief and maintaining quality of life while emphasizing the patient's and family's rights to participate in informed discussion and to make choices. This patient- and family-centered approach uses the skills of interdisciplinary team members to provide a comprehensive continuum of care including spiritual and emotional needs.

PANCREAS: A gland situated near the stomach that secretes a digestive fluid into the intestine through one or more ducts and also secretes the hormone insulin.

PANCREATITIS: Inflammation of the pancreas (see) that can produce severe pain and debilitating illness. An occasional side effect of treatment with ddI (see), can result in severe abdominal pain and death. Its onset can be predicted by rises in blood levels of the pancreatic enzyme, amylase.

PANCYTOPENIA: Deficiency of all cell elements of the blood.

PANDEMIC: A disease prevalent throughout an entire country, continent, or the whole world. See Epidemic.

PAP SMEAR: A method for the early detection of cancer and other abnormalities of the female genital tract, especially of the cervix (see), employing scraped as well as exfoliated cells (cells that have been shed into the vaginal fluid) and a special staining technique for microscopic examination that differentiates diseased tissue. Also known as Papanicolaou Smear after George Papanicolaou, the American cytologist who developed this method.

PAPILLOMA: 1. A benign tumor (as a wart or condyloma) resulting from an overgrowth of epithelial tissue on papillae of vascularized connective tissue (as of the skin). 2. An epithelial tumor caused by a virus. See Condyloma; Epithelium; JC Virus.

PARALLEL TRACK: A system of distributing experimental drugs to patients who are unable to participate in ongoing clinical efficacy trials and have no other treatment options. See Clinical Trial.

PARASITE: A plant or animal that lives and feeds on or within another living organism (host), causing some degree of harm to the host organism.

PARENCHYMA: The tissue of an organ (as distinguished from supporting or connective tissue).

PARENTERAL: Not in or through the digestive system. For example, parenteral can pertain to blood being drawn from a vein in the arm or introduced into that vein via a transfusion (intravenous), or to injection

of medications or vaccines through the skin (subcutaneous) or into the muscle (intramuscular).

PARESTHESIA: Abnormal sensations such as burning, tingling, or a "pins-and-needles" feeling. Paresthesia may constitute the first group of symptoms of peripheral neuropathy (see), or it may be a limited drug side effect that does not worsen with time. Circumoral paresthesia affects the area around the mouth.

PASSIVE IMMUNITY: Also referred to as acquired immunity. Resistance resulting from previous exposure to an infectious agent or antigen (see) may be active (see active immunity) or passive. Passive immunity can be acquired from the transfer of antibodies from another person or from an animal, either naturally—as from mother to fetus—or by intentional inoculation. The latter is also called artificial passive immunity. Passive immunity is specific with respect to the particular antibodies transferred. Passive, cell-mediated immunity produced by the transfer of living lymphoid cells from an immune animal to a normal one is sometimes referred to as adoptive immunity.

PASSIVE IMMUNOTHERAPY: Process in which individuals with advanced disease (who have low levels of HIV antibody production) are infused with plasma rich in HIV antibodies or an immunoglobulin concentrate (HIVIG) from such plasma. The plasma is obtained from asymptomatic HIV-positive individuals with high levels of HIV antibodies.

PATHOGEN: Any disease-producing microorganism or material.

PATHOGENESIS: The origin and development of a disease.

PBMC: See Peripheral Blood Mononuclear Cell.

PCP: See *Pneumocystis carinii* Pneumonia.

PCR: See Polymerase Chain Reaction.

PEDIATRIC AIDS CLINICAL TRIALS GROUP (PACTG): This is the preeminent organization in the world for evaluating treatments for HIV-infected children and adolescents, and for developing new approaches for the interruption of mother-to-infant transmission. It has set the standards of care for children infected with HIV and for the interruption of vertical transmission. **Internet address: http://pactg.s-3.com/.**

PELVIC INFLAMMATORY DISEASE (PID): Gynecological condition caused by an infection (usually sexually transmitted) that spreads from the vagina to the upper parts of a woman's reproductive tract in the pelvic cavity. PID takes different courses in different women, but can cause abscesses and constant pain almost anywhere in the genital tract. If left untreated, it can cause infertility or more frequent periods. Severe cases may even spread to the liver and kidneys causing dangerous internal bleeding and death.

PEPTIDE: (Also polypeptide.) Biochemical formed by the linkage of up to about 50 amino acids (see) to form a chain. Longer chains are called proteins. The amino acids are coupled by a peptide bond, a special linkage in which the nitrogen atom of one amino acid binds to the carboxyl carbon atom of another. Many peptides, such as the hormones vasopressin and ACTH, have physiological or antibacterial activity.

PERIANAL: Around the anus.

PERINATAL: Events that occur at or around the time of birth.

PERINATAL TRANSMISSION: Transmission of a pathogen, such as HIV, from mother to baby before, during, or after the birth process. Ninety percent of children reported with AIDS acquired HIV infection from their HIV-infected mothers.

PERIPHERAL BLOOD MONONUCLEAR CELL (PBMC): Cells in the bloodstream with one nucleus (see). Generally refers to lymphocytes (see) and macrophages (see).

PERIPHERAL NEURITIS: Inflammation of terminal nerves or the nerve endings, usually associated with pain, muscle wasting, and loss of reflexes.

PERIPHERAL NEUROPATHY: Condition characterized by sensory loss, pain, muscle weakness, and wasting of muscle in the hands or legs and feet. It may start with burning or tingling sensations or numbness in the toes and fingers. In severe cases, paralysis may result. Peripheral neuropathy may arise from an HIV-related condition or be the side effect of certain drugs, some of the nucleoside analogs (see) in particular.

PERSISTENT GENERALIZED LYMPHADENOPATHY (PGL): Chronic, diffuse, noncancerous lymph node enlargement. Typically it has been found in persons with persistent bacterial, viral, or fungal infections. PGL in HIV infection is a condition in which lymph nodes are chronically swollen in at least two areas of the body for 3 months or more with no obvious cause other than the HIV infection.

PGL: See Persistent Generalized Lymphadenopathy.

PHA: See phytohemagglutinin.

PHAGOCYTE: A cell that is able to ingest and destroy foreign matter, including bacteria.

PHAGOCYTOSIS: The process of ingesting and destroying a virus or other foreign matter by phagocytes. See Macrophage; Monocyte.

PHARMACOKINETICS: The processes (in a living organism) of absorption, distribution, metabolism, and excretion of a drug or vaccine.

PHASE I TRIALS: Involve the initial introduction of an investigational new drug into humans. Phase I trials are closely monitored and may be conducted in patients or in healthy volunteers. The studies are designed to determine the metabolism and pharmacologic actions of the drug in humans, safety, side effects associated with increasing doses, and if possible, early evidence of effectiveness. The trials also

can include studies of structure-activity relationships, mechanisms of action in humans, use of the investigational drug as research tools to explore biological phenomena, or disease processes. The total number of patients included in Phase I studies varies but is generally in the range of 20 to 80. Sufficient information should be obtained in the trial to permit design of well-controlled, scientifically valid Phase II studies.

PHASE II TRIALS: Include controlled clinical studies of effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study, and determination of common, short-term side effects and risks associated with the drug. Phase II studies are typically well controlled, closely monitored, and usually involve no more than several hundred patients.

PHASE III TRIALS: Expanded controlled and uncontrolled studies. They are performed after preliminary evidence of drug effectiveness has been obtained. They are intended to gather additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide adequate basis for physician labeling. These studies usually include anywhere from several hundred to several thousand subjects.

PHASE IV TRIALS: Post-marketing studies, carried out after licensure of the drug. Generally, a Phase IV trial is a randomized, controlled trial that is designed to evaluate the long-term safety and efficacy of a drug for a given indication. Phase IV trials are important in evaluating AIDS drugs because many drugs for HIV infection have been given accelerated approval with small amounts of clinical data about the drugs' effectiveness.

PHENOTYPIC ASSAY: A procedure whereby a sample DNA (see) of a patient's HIV is tested against various antiretroviral (see) drugs to see if the virus is susceptible or resistant to these drug(s). See also Resistance.

PHOTOSENSITIVITY: Heightened skin response to sunlight or ultraviolet light (rapid burning when exposed to the sun).

PHS: See Public Health Service.

PHYTOHEMAGGLUTININ: A plant chemical used to stimulate the multiplication (proliferation) of T lymphocytes (see T Cells) in laboratory tests.

PITUITARY GLAND: Small, oval endocrine gland that lies at the base of the brain. It is called the master gland because the other endocrine glands depend on its secretions for stimulation. The pituitary has two distinct lobes, anterior and posterior. The anterior lobe secretes at least six hormones: human growth hormone, which stimulates overall body growth: ACTH (adrenocorticotropic hormone), which controls steroid hormone secretion by the adrenal cortex; thyrotropic hormone, which stimulates the activity of the thyroid gland; and three gonadotropic hormones, which control growth and reproductive activity of the gonads (ovaries and testes). The posterior lobe secretes an antidiuretic hormone, which causes water retention by the kidneys, and oxytocin, which stimulates the mammary glands to release milk and also causes uterine contractions. An overactive pituitary during childhood can cause gigantism. Dwarfism results from pituitary deficiency in childhood.

PLACEBO: An inactive substance (may look like the real medication) against which investigational treatments are compared for efficacy and safety. See Placebo Controlled Study.

PLACEBO CONTROLLED STUDY: A method of investigation of drugs in which an inactive substance (the placebo) is given to one group of patients, while the drug being tested is given to another group. The results obtained in the two groups are then compared to see if the investigational treatment is more effective in treating the condition.

PLACEBO EFFECT: A physical or emotional change, occurring after a substance is taken or administered, that is not the result of any special property of the substance. The change may be beneficial, reflecting the

expectations of the patient and, often, the expectations of the person giving the substance.

PLASMA: That 10 percent of the blood that contains nutrients, electrolytes (dissolved salts), gases, albumin, clotting factors, wastes, and hormones.

PLASMA CELLS: Large antibody-producing cells that develop from B cells. See Antibodies; B Lymphocytes.

PLASMAPHERESIS: The selective removal of certain proteins or antibodies from the blood (followed by reinjection of the blood).

PLATELETS: Active agents of inflammation when damage occurs to a blood vessel. They are not actually cells, but fragments released by megakaryocyte cells. Megakaryocyte is a large cell in the bone marrow whose function is to produce platelets. When vascular damage (i.e., damage to blood vessels) occurs, the platelets stick to the vascular walls, forming clots to prevent the loss of blood. Thus, it is important to have adequate numbers of normally functioning platelets to maintain effective coagulation (clotting) of the blood. There are drugs that can potentially alter the platelet count, making it necessary to monitor the count. Also, some persons living with HIV develop thrombocytopenia—a condition characterized by a platelet count of less than 100,000 platelets per cubic millimeter of blood. The normal value for men is 154,000–354,000 platelets per cubic millimeter of blood. For women, it is 162,000–380,000 platelets per cubic millimeter of blood.

PML: See Progressive Multifocal Leukoencephalopathy.

PNEUMOCYSTIS CARINII PNEUMONIA (PCP): An infection of the lungs caused by *Pneumocystis carinii,* which is thought to be a protozoa but may be more closely related to a fungus. *P. carinii* grows rapidly in the lungs of persons with AIDS and is a frequent AIDS- related cause of death. *P. carinii* infection sometimes may occur

elsewhere in the body (skin, eye, spleen, liver, or heart). The standard treatment for persons with PCP is either a combination of trimethoprim and sulfamethoxazole (TMP/SMX, also called Bactrim or Septra), dapsone, or pentamidine.

POL: *(pol)* A gene of HIV that codes for the enzymes protease, reverse transcriptase and integrase (see entries for these terms).

POLYMERASE: Any of several enzymes (see) that catalyze the formation of DNA (see) or RNA (see) from precursor substances in the presence of preexisting DNA or RNA acting as templates (i.e., patterns).

POLYMERASE CHAIN REACTION (PCR): 1. A laboratory process that selects a DNA segment from a mixture of DNA chains and rapidly replicates it; used to create a large, readily analyzed sample of a piece of DNA. It is used in DNA fingerprinting and in medical tests to identify diseases from the infectious agent's DNA. See DNA. 2. As related to HIV—also called RT-PCR—a sensitive laboratory technique that can detect and quantify HIV in a person's blood or lymph nodes. PCR works by repeatedly copying genetic material using heat cycling and enzymes similar to those used by cells. It is an FDA-approved test to measure viral load (see).

POLYNEURITIS: Inflammation of many nerves at once.

POLYPEPTIDE: See Peptide.

POLYVALENT VACCINE: A vaccine that is active against multiple viral strains.

PPD TEST: See Purified Protein Derivative.

PRECLINICAL: Refers to the testing of experimental drugs in the test tube or in animals—the testing that occurs before trials in humans may be carried out.

PRECURSOR CELLS: Cells from which natural processes form other cells.

PREVALENCE: A measure of the proportion of people in a population affected with a particular disease at a given time.

PRIMARY HIV INFECTION: See Acute HIV Infection.

PRIMARY ISOLATE: HIV taken from an infected individual (as opposed to grown in laboratory cultures).

PROCTITIS: Inflammation of the rectum.

PRODROME: A symptom that indicates the onset of a disease.

PRODRUG: An inactive or partially active drug that is metabolically changed in the body to an active drug.

PROGENITOR: Parent or ancestor.

PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML): A rapidly debilitating opportunistic infection (see) caused by the JC virus (see) that infects brain tissue and causes damage to the brain and the spinal cord. Symptoms vary from patient to patient but include loss of muscle control, paralysis, blindness, problems with speech, and an altered mental state. PML can lead to coma and death. In some cases, HAART regimens using medications known to cross the blood-brain barrier are used to treat PML. Other studies are ongoing to determine the usefulness of other medications, such as cidofovir and topotecan HCL, in the treatment of PML.

PROPHYLACTIC DRUG: A drug that helps to prevent a disease or initial infection. For example, the drug Bactrim is used as a prophylactic treatment for PCP (see). See also Prophylaxis.

PROPHYLAXIS: Treatment to prevent the onset of a particular disease ("primary" prophylaxis), or the recurrence of symptoms in an existing infection that has been brought under control ("secondary" prophylaxis, maintenance therapy).

PROTEASE: An enzyme (see) that breaks down proteins (see) into their component peptides. HIV's protease enzyme breaks apart long strands of viral protein into the separate proteins making up the viral core. The enzyme acts as new virus particles are budding off a cell membrane. Protease is the first HIV protein whose three-dimensional structure has been characterized. See Proteins.

PROTEASE INHIBITORS: Antiviral drugs that act by inhibiting the virus' protease (see) enzyme, thereby preventing viral replication. Specifically, these drugs block the protease enzyme from breaking apart long strands of viral proteins to make the smaller, active HIV proteins that comprise the virion (see). If the larger HIV proteins are not broken apart, they cannot assemble themselves into new functional HIV particles. FDA has approved the following protease inhibitors as drugs to treat HIV disease: Saquinavir (Invirase, Fortovase), Indinavir (Crixivan), Nelfinavir (Viracept), Ritonavir (Norvir), and Amprenavir (Agenerase).

PROTEINS: Highly complex organic compounds found in all living cells. Protein is the most abundant class of all biological molecules, comprising about 50 percent of cellular dry weight. Structurally, proteins are large molecules composed of one or more chains of varying amounts of the same 22 amino acids (see) that are linked by peptide bonds. Each protein is characterized by a unique and invariant amino acid sequence. The information for the synthesis of the specific amino acid sequence in a protein, from free amino acids, is carried by the cell's nucleic acid (see).

PROTOCOL: The detailed plan for conducting a clinical trial (see). It states the trial's rationale, purpose, drug or vaccine dosages, length of study, routes of administration, who may participate (see inclusion/exclusion criteria), and other aspects of trial design.

PROTOZOA: Large group of one-celled (unicellular) animals, including amoebas. Some protozoa cause parasitic diseases in persons with

AIDS, notably toxoplasmosis (see) and cryptosporidiosis (see). See *Pneumocystis carinii* Pneumonia.

PROVIRUS: Viral genetic material, in the form of DNA (see) that has been integrated into the host genome. HIV, when it is dormant in human cells, is in a proviral form.

PRURITIS: Itching.

PSEUDOVIRION: A virus-like particle.

PULMONARY: Pertaining to the lungs.

PURIFIED PROTEIN DERIVATIVE (PPD): Material used in the tuberculin skin test (TST; see); the most common test for exposure to *Mycobacterium tuberculosis*, the bacterium that causes TB. PPD is sometimes used synonymously with TST. In the PPD test, a small amount of protein from TB is injected under the skin. If patients have been previously infected, they will mount a delayed-type hypersensitivity reaction, characterized by a hard red bump called an induration.

RADIOLOGY: The science of diagnosis and/or treatment using radiant energy. Includes x- rays, CT scan (see), and destruction of tumors by radiation.

RANDOMIZED TRIAL: A study in which participants are randomly (i.e., by chance) assigned to one of two or more treatment arms (see) or regimen of a clinical trial (see). Occasionally placebos (see) are utilized. Randomization minimizes the differences among groups by equally distributing people with particular characteristics among all the trial arms.

REACTOGENICITY: The capacity to produce adverse reactions.

RECEPTOR: A molecule on the surface of a cell that serves as a recognition or binding site for antigens (see), antibodies (see), or other cellular or immunological components.

RECOMBINANT: An organism whose genome (see) contains integrated genetic material from a different organism. Also used in relation to compounds produced by laboratory or industrial cultures of genetically engineered living cells (see Genetic Engineering). The cells' genes have been altered to give the capability of producing large quantities of the desired compound for use as a medical treatment. Recombinant compounds often are altered versions of naturally occurring substances.

RECOMBINANT DNA: See Biotechnology; Genetic Engineering.

RECOMBINANT DNA TECHNOLOGY: See Genetic Engineering.

REFRACTORY: Referring to a disease that does not readily respond to treatment.

REGULATORY GENES: As related to HIV: Three regulatory HIV genes—*tat*, *rev*, and *nef*—and three so-called auxiliary genes *vif*, *vpr*,

and *vpu*—contain information for the production of proteins that regulate the virus's ability to infect a cell, produce new copies of the virus, or cause disease. See *nef; rev; tat.*

REGULATORY T CELLS: T cells that direct other immune cells to perform special functions. The chief regulatory cell, the CD4+ T cell (see) or T helper cell, is HIV's chief target.

REMISSIONS: The lessening of the severity or duration of outbreaks of a disease, or the abatement (diminution in degree or intensity) of symptoms altogether over a period of time.

RENAL: Pertaining to the kidneys.

RESCRIPTOR: See Delavirdine.

RESISTANCE: Reduction in a pathogen's sensitivity to a particular drug. Resistance is thought to result usually from a genetic mutation (see). In HIV, such mutations can change the structure of viral enzymes (see) and proteins (see) so that an antiviral drug can no longer bind with them as well as it used to. Resistance detected by searching a pathogen's genetic makeup for mutations thought to confer lower susceptibility is called "genotypic resistance." Resistance that is found by successfully growing laboratory cultures of the pathogen in the presence of a drug is called "phenotype resistance."

RETICULOENDOTHELIAL CELLS: A system of interstitial cells that includes all the phagocytic cells, which trap and consume foreign agents, except the leukocytes (see) circulating in the bloodstream. This system forms a network throughout the body and is another of the body's defense systems against invading organisms in the connective tissues of the body. See Phagocyte.

RETINA: Light-sensitive tissue at the back of the eye that transmits visual impulses via the optic nerve to the brain. See Retinitis.

RETINAL DETACHMENT: Condition in which a portion of the retina (see) becomes separated from the inner wall of the eye. In AIDS

patients, it can result from retinal disease such as CMV retinitis (see). The condition can rapidly lead to vision loss but is treatable by adding silicone to the eye's vitreous humor to increase the pressure on the retina.

RETINITIS: Inflammation of the retina (see), linked in AIDS to cytomegalovirus (CMV; see) infection. Untreated, it can lead to blindness.

RETROVIR: See Zidovudine.

RETROVIRUS: A type of virus that, when not infecting a cell, stores its genetic information on a single-stranded RNA (see) molecule instead of the more usual double-stranded DNA (see). HIV is an example of a retrovirus. After a retrovirus penetrates a cell, it constructs a DNA version of its genes using a special enzyme called reverse transcriptase (see). This DNA then becomes part of the cell's genetic material.

REV: *(rev)* One of the regulatory genes of HIV. Three HIV regulatory genes—*tat*, *rev*, and *nef*—and three so-called auxiliary genes—*vif*, *vpr*, and *vpu*—contain information necessary for the production of proteins that control the virus's ability to infect a cell, produce new copies of the virus, or cause disease. See *nef*; *tat*.

REVERSE TRANSCRIPTASE: This enzyme of HIV—and other retroviruses (see)—converts the single-stranded viral RNA (see) into DNA (see), the form in which the cell carries its genes. Some antiviral drugs approved by the FDA for the treatment of HIV infection (e.g., AZT, ddC, ddI, 3TC, D4T, and abacavir) work by interfering with this stage of the viral life cycle. They are also referred to as reverse transcriptase inhibitors (RTIs).

RIBONUCLEIC ACID (RNA): 1. A nucleic acid, found mostly in the cytoplasm—rather than the nucleus—of cells, that is important in the synthesis of proteins. The amount of RNA varies from cell to cell. RNA, like the structurally similar DNA (see), is a chain made up of subunits called nucleotides (see). In protein synthesis, messenger RNA (mRNA;

see) replicates the DNA code for a protein and moves to sites in the cell called ribosomes (see). There, transfer RNA (tRNA) assembles amino acids to form the protein specified by the messenger RNA. Most forms of RNA (including messenger and transfer RNA) consist of a single nucleotide strand, but a few forms of viral RNA that function as carriers of genetic information (instead of DNA) are double-stranded. Some viruses, such as HIV, carry RNA instead of the more usual genetic material DNA. See Cytoplasm; Retrovirus.

RIBOSOME: A cytoplasmic organelle (see), composed of ribonucleic acid (see) and protein, that functions in the synthesis of protein. Ribosomes interact with messenger RNA (mRNA; see) and transfer RNA to join together amino acid units into a polypeptide (see) chain according to the sequence determined by the genetic code.

RITONAVIR: A protease inhibitor (see) first approved by FDA in 1996 for use alone or in combination with nucleoside analogs (see) for the treatment of HIV infection in adults and children 2 years of age and older. Also called Norvir.

RNA: See Ribonucleic Acid.

ROUTE OF ADMINISTRATION: See Administration.

RTI: (Reverse Transcriptase Inhibitors). See Reverse Transcriptase.

RT-PCR: (Reverse Transcriptase Polymerase Chain Reaction). An FDA-approved test to measure viral load (see). The test is also known as PCR (Polymerase Chain Reaction; see).

RYAN WHITE C.A.R.E. ACT: Through the Ryan White Comprehensive AIDS Resources Emergency (C.A.R.E.) Act, health care and support services are provided for persons living with HIV/AIDS. HRSA (see) administers this Act, which was reauthorized by Congress in 1996 for 5 years. The metropolitan areas most affected by the HIV epidemic are awarded Title I grants to improve and expand health care. Title II

grants to states and territories support essential health care and support services for persons living with HIV/AIDS, including health insurance and AIDS Drug Assistance Programs (see). Title III(b) supports early intervention in clinical settings such as community and migrant health centers, health care for the homeless programs, and Native Hawaiian health programs. Title IV supports services for women, children, adolescents, and families affected by the HIV epidemic. Part F of the Act supports Special Projects of National Significance (SPNS) (see) and AIDS Education and Training Centers (AETCs) (see).

SALMONELLA: A family of gram-negative (see) bacteria, found in undercooked poultry or eggs, that are a common cause of food poisoning, and that can cause serious disseminated disease in HIV-positive persons.

SALVAGE THERAPY: A treatment effort for people who are not responding to, or cannot tolerate the preferred, recommended treatments for a particular condition. In the context of HIV infection, drug treatments that are used or studied in individuals who have failed one or more HIV drug regimens, including protease inhibitors (see). In this case, failed refers to the inability to achieve and sustain low viral load levels.

SAMHSA: See Substance Abuse and Mental Health Services Administration.

SAQUINAVIR: 1. An FDA approved (12/07/95) hard-gel capsule protease inhibitor (see) for combination use with nucleoside analogs (see) for the treatment of HIV infection. Also called Invirase. 2. An FDA approved (11/07/97) soft-gel capsule protease inhibitor (see) for use in combination with other antiretroviral agents (see) for the treatment of HIV infection. Also called Fortovase.

SARCOMA: A malignant (cancerous) tumor of the skin and soft tissue.

SEBORRHEIC DERMATITIS: A chronic inflammatory disease of the skin of unknown cause or origin, characterized by moderate erythema (see); dry, moist, or greasy scaling; and yellow crusted patches on various areas, including the mid-parts of the face, ears, supraorbital regions (above the orbit of the eye), umbilicus (the navel), genitalia, and especially the scalp. Seborrheic dermatitis in patients infected with HIV responds to a variety of therapies but tends to reoccur. Topic antifungal

agents and corticosteroids suppress the process, but therapy must be applied repeatedly.

SEPSIS: The presence of harmful microorganisms or associated toxins in the blood.

SEROCONVERSION: The development of antibodies (see) to a particular antigen (see). When people develop antibodies to HIV, they "seroconvert" from antibody-negative to antibody-positive. It may take from as little as 1 week to several months or more after infection with HIV for antibodies to the virus to develop. After antibodies to HIV appear in the blood, a person should test positive on antibody tests. See Incubation Period; Window Period.

SEROLOGIC TEST: Any of a number of tests that are performed on the clear portion of blood (serum; see). Often refers to a test that determines the presence of antibodies (see) to antigens (see) such as viruses.

SEROPREVALENCE: As related to HIV infection, the proportion of persons who have serologic (i.e., pertaining to serum) evidence of HIV infection at any given time. See Serum.

SEROSTATUS: Results of a blood test for specific antibodies (see).

SERUM: The clear, thin, and sticky fluid portion of the blood that remains after coagulation (clotting). Serum contains no blood cells, platelets, or fibrinogen.

SEXUALLY TRANSMITTED DISEASE (STD): Also called venereal disease (VD) (an older public health term) or sexually transmitted infections (STIs). Sexually transmitted diseases are infections spread by the transfer of organisms from person to person during sexual contact. In addition to the "traditional" STDs (syphilis and gonorrhea), the spectrum of STDs now includes HIV infection, which causes AIDS; *Chlamydia trachomatis* infections; human papilloma virus (HPV) infection; genital herpes; chancroid; genital mycoplasmas; hepatitis B; trichomoniasis; enteric infections; and ectoparasitic diseases (i.e.,

diseases caused by organisms that live on the outside of the host's body). See entries for most of these terms. The complexity and scope of STDs have increased dramatically since the 1980s; more than 20 organisms and syndromes are now recognized as belonging in this category.

SF-2: A strain of HIV used in vaccine development.

SGOT: (Serum Glutamic Oxaloacetic Transaminase.) Also known as AST (aspartate aminotransaminase), a liver enzyme that plays a role in protein metabolism, such as SGPT (see). Elevated serum levels of SGOT are a sign of liver damage from disease or drugs.

SGPT: (Serum Glutamic Pyruvate Transaminase.) Also known as ALT (alanine aminotransaminase), a liver enzyme that plays a role in protein metabolism like SGOT (see). Elevated serum levels of SGPT are a sign of liver damage from disease or drugs.

SHINGLES: See Herpes Varicella Zoster Virus.

SHIV: Genetically engineered hybrid virus having an HIV envelope and an SIV core. See Genetic Engineering; Hybrid; Simian Immunodeficiency Virus (SIV).

SIDE EFFECTS: The actions or effects of a drug (or vaccine) other than those desired. The term usually refers to undesired or negative effects, such as headache, skin irritation, or liver damage. Experimental drugs must be evaluated for both immediate and long-term side effects.

SIMIAN IMMUNODEFICIENCY VIRUS (SIV): An HIV-like virus that infects monkeys, chimpanzees, and other non-human primates.

SINUSITIS: Inflammation of the nasal cavity and sinuses.

SIV: See Simian Immunodeficiency Virus.

SPECIAL PROJECTS OF NATIONAL SIGNIFICANCE (SPNS): The SPNS Program is the research and demonstration program of the Ryan White C.A.R.E. Act (see). The program's mission is to advance

knowledge and skills in health and support services for persons with HIV/AIDS. The authorizing legislation specifies three objectives for this program: (1) to assess the effectiveness of particular models of care, (2) to support innovative program design, and (3) to promote replication of effective models.

SPINAL TAP: See Lumbar Puncture.

SPLEEN: Large lymphatic organ in the upper left of the abdominal cavity with several functions: (1) trapping of foreign matter in the blood, (2) destruction of degraded red blood cells and foreign matter by macrophages (see), (3) formation of new lymphocytes (see) and antibody production, and (4) storage of excess red blood cells.

SPLENOMEGALY: An enlarged spleen.

SPUTUM ANALYSIS: Method of detecting certain infections (especially tuberculosis) by culturing of sputum—the mucus matter that collects in the respiratory and upper digestive passages and is expelled by coughing.

STANDARDS OF CARE: Treatment regimen or medical management based on state-of-the-art patient care.

STAPHYLOCOCCUS: Type of bacteria that may cause various types of infections.

STAVUDINE: A nucleoside reverse transcriptase inhibitor (see) first approved by FDA in 1994 and used for the treatment of adults and children with HIV infection who have undergone prolonged prior AZT (see) therapy. Also called d4T, Zerit.

STD: See Sexually Transmitted Disease.

STEM CELLS: Cells from which all blood cells derive. Bone marrow is rich in stem cells. Clones of stem cells may become any one of the repertoires of immune cells depending upon which cytokines (see) and hormones they are exposed to.

STERILIZING IMMUNITY: An immune response that completely eliminates an infection.

STEROID: Member of a large family of structurally similar lipid (see) substances. Steroid molecules have a basic skeleton consisting of four interconnected carbon rings. Different classes of steroids have different functions. All the natural sex hormones are steroids. Anabolic steroids increase muscle mass. Antiinflammatory steroids (or corticosteroids) can reduce swelling, pain, and other manifestations of inflammation.

STEVENS–JOHNSON SYNDROME: A severe and sometimes fatal form of erythema multiforme (see) that is characterized by severe skin manifestations; conjunctivitis (eye inflammation), which often results in blindness; Vincent's angina (trench mouth); and ulceration of the genitals and anus.

STOMATITIS: Any of numerous inflammatory diseases of the mouth having various causes, such as mechanical trauma, irritants, allergy, vitamin deficiency, or infection.

STRAIN: Subgroup of a species (also called taxon).

STRATIFICATION: A layered configuration.

SUBARACHNOID SPACE: The space through which the spinal fluid circulates.

SUBCLINICAL INFECTION: An infection, or phase of infection, without readily apparent symptoms or signs of disease.

SUBCUTANEOUS (SQ): Beneath the skin or introduced beneath the skin (e.g., subcutaneous injections).

SUBSTANCE ABUSE AND MENTAL HEALTH SERVICES ADMINISTRATION (SAMHSA): An agency of the U.S. Department of Health and Human Services (see). SAMHSA's mission within the Nation's health system is to improve the quality and availability of prevention, treatment, and rehabilitation services in order to reduce

illness, death, disability, and cost to society resulting from substance abuse and mental illnesses. **Internet address: http://www.samhsa.gov/.**

SUBUNIT HIV VACCINE: A genetically engineered vaccine that is based on only part of the HIV molecule. See Genetic Engineering.

SULFA DRUG: A sulfonamide (see) drug used to treat bacterial infections. These drugs inhibit the action of p-aminobenzoic acid, a substance bacteria need in order to reproduce. Sulfa drugs are now used primarily in the treatment of urinary tract infections and ulcerative colitis. In the HIV area, the sulfa drug, sulfadiazine, is used in combination with pyrimethamine as standard therapy for toxoplasmosis (see). Trimethoprim is used in combination with another sulfa drug, sulfamethoxazole against PCP (see).

SULFONAMIDES: Synthetic derivatives of p-aminobenzenesulfonamide. See Sulfa Drug.

SUPERANTIGEN: Investigators have proposed that a molecule known as a superantigen, made by either HIV or an unrelated agent, may stimulate massive quantities of CD4+ T (see) cells at once, rendering them highly susceptible to HIV infection and subsequent cell death. See Antigen.

SUPPRESSOR PHENOMENON: Process where CD8+ cells not only kill HIV-infected cells directly by a process called cytolysis, but also secrete soluble factors that suppress HIV replication in both blood and lymph nodes. It appears that CD8+ cells secrete signaling molecules, called beta-chemokines (see chemokines), which normally recruit inflammatory cells to the site of an infection. Three of these beta-chemokines, RANTES, MIP–1a, and MIP–1b, appear to block HIV replication by occupying receptors necessary for the entry of some strains of HIV into their target cells.

SUPPRESSOR T CELLS: (T8, CD8.) Subset of T cells (see) that halts antibody (see) production and other immune responses.

SURROGATE MARKER: Laboratory tests that may predict a patient's clinical outcome or indicate whether a drug is effective without having to rely on the traditional clinical endpoints of death or development of a major opportunistic infection. See CD4 (T4) or CD4+ Cells; CD8 (T8) Cells.

SURVEILLANCE: See Epidemiologic Surveillance.

SUSCEPTIBLE: Vulnerable or predisposed to a disease.

SUSTIVA: See Efavirenz.

SYMPTOMS: Any perceptible, subjective change in the body or its functions that indicates disease or phases of disease, as reported by the patient.

SYNCYTIA: ("Giant Cells.") Dysfunctional multicellular clumps formed by cell-to-cell fusion. Cells infected with HIV may also fuse with nearby uninfected cells, forming balloonlike giant cells called syncytia. In test tube experiments, these giant cells have been associated with the death of uninfected cells. The presence of so-called syncytia-inducing variants of HIV has been correlated with rapid disease progression in HIV-infected individuals.

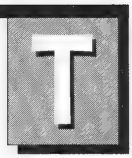
SYNDROME: A group of symptoms as reported by the patient and signs as detected in an examination that together are characteristic of a specific condition.

SYNERGISM, SYNERGISTIC: An interaction between two or more treatments (e.g., drugs) that produces or enhances an effect that is greater than the sum of the effects produced by the individual treatments.

SYNTHESIS: 1. In chemistry, the formation of a compound from simpler compounds or elements. 2. The production of a substance (e.g., as in protein synthesis) by the union of chemical elements, groups, or simpler compounds, or by the degradation (i.e., breaking down) of a complex compound.

SYPHILIS: A disease—primarily sexually transmitted—resulting from infection with the spirochete (a bacterium), *Treponema pallidum*. Syphilis can also be acquired in the uterus during pregnancy.

SYSTEMIC: Concerning or affecting the body as a whole. A systemic therapy is one that the entire body is exposed to, rather than just the target tissues affected by a disease.



3TC: See Lamivudine.

TAT: *(tat)* One of the regulatory genes of HIV. Three HIV regulatory genes—*tat*, *rev*, and *nef*—and three so-called auxiliary genes—*vif*, *vpr*, and *vpu*—contain information necessary for the production of proteins that control the virus' ability to infect a cell, produce new copies of the virus, or cause disease. The tat gene is thought to enhance virus replication. See *nef*; *rev*.

TB: See Tuberculosis.

T CELLS: (T Lymphocytes.) T cells are white blood cells, derived from the thymus gland (see), that participate in a variety of cell-mediated immune reactions. Three fundamentally different types of T cells are recognized: helper, killer (see killer T cells), and suppressor. They are the immune system's "border police," responsible for finding infected or cancerous cells. The killer T cell receptors (TCR) bind to an infected cell's distress signal—a combination of one of the cell's own proteins and a tiny fragment of the invader's protein. The bits of foreign protein are made with the help of enzymes inside the invaded cell that chew up the pathogens into protein fragments (peptides), which are then scooped up by the major histocompatibility complex (MHC; see) and carted through the cell membrane.

T4 CELL: (Also called T-helper cell). Antibody-triggered immune cells that seek and attack invading organisms. Macrophages (see) summon T4 cells to the infection site. There the T4 cell reproduces and secretes its potent lymphokines (see) that stimulate B cell (see) production of antibodies; signal natural killer or cytotoxic (cell-killing) T cells (see); and summon other macrophages to the infection site. In healthy immune systems, T4 cells are twice as common as T8 cells. If a person has AIDS, the proportion is often reversed. The virus enters T4 cells

through its receptor protein and encodes its genetic information into the host cell's DNA, making T cells virtual viral factories. HIV-infected T4 cells may not die, but, rather, may cease to function. They also begin to secrete a substance known as Soluble Suppressor Factor that inhibits the functioning of even unaffected T cells.

T8 CELL: (Also called killer cells; see Cytotoxic T-lymphocyte). Immune cells that shut down the immune response after it has effectively wiped out invading organisms. Sensitive to high concentrations of circulating lymphokines (see), T8 cells release their own lymphokines when an immune response has achieved its goal, signaling all other participants to cease their coordinated attack. A number of B lymphocytes (see) remain in circulation in order to fend off a possible repeat attack by the invading organism. With HIV, however, the immune system's response system does not work. T4 cells (see) are dysfunctional, lymphokines proliferate in the bloodstream, and T8 cells compound the problem by misreading the oversupply of lymphokines as meaning that the immune system has effectively eliminated the invader. So while HIV is multiplying, T8 cells are simultaneously attempting to further shut down the immune system. The stage is set for normally repressed infectious agents, such as PCP (see) or CMV (see), to proliferate unhindered and to cause disease.

TEMPLATE: A gauge, pattern, or mold used as a guide to the form of the piece being made. In biology, a molecule—such as DNA—that serves as a pattern for the generation of another macromolecule (e.g., messenger RNA). See Ribonucleic Acid.

TERATOGENICITY: The production of physical defects in offspring in utero (i.e., causing birth defects). Teratogenicity is a potential side effect of some drugs, such as thalidomide.

TERRY BEIRN COMMUNITY PROGRAMS FOR CLINICAL RESEARCH ON AIDS: See Community Programs for Clinical Research on AIDS.

TESTOSTERONE: Naturally occurring male hormone. When administered as a drug it can cause gain in lean body mass, increased sex drive, and possibly aggressive behavior. Many men with HIV have low testosterone levels.

THERAPEUTIC HIV VACCINE: Also called treatment vaccine. A vaccine designed to boost the immune response to HIV in persons already infected with the virus. A therapeutic vaccine is different from a preventive vaccine, which is designed to prevent a disease from becoming established in a person.

TH1 RESPONSE: An acquired immune response (see) whose most prominent feature is high cytotoxic T lymphocyte (see) activity relative to the amount of antibody (see) production. The Th1 response is promoted by CD4+ "Th1" T-helper cells. See Th2 Response.

TH2 RESPONSE: An acquired immune response (see) whose most prominent feature is high antibody production relative to the amount of cytotoxic T lymphocyte activity. The Th2 response is promoted by CD4+ "Th2" T-helper cells. See Th1 Response.

THROMBOCYTOPENIA: A decreased number of blood platelets (cells important for blood clotting). See Platelets; Immune Thrombocytopenia Purpura.

THRUSH: Sore patches in the mouth caused by the fungus *Candida albicans*. Thrush is one of the most frequent early symptoms or signs of an immune disorder. The fungus commonly lives in the mouth, but only causes problems when the body's resistance is reduced either by antibiotics that have reduced the number of competitive organisms in the mouth, or by an immune deficiency such as HIV disease. See Candidiasis.

THYMOSIN: A polypeptide hormone of the thymus (see) gland that influences the maturation of T cells (see) destined for an active role in cell-mediated immunity.

THYMUS: A mass of glandular tissue (lymphoid organ) found in the upper chest under the breastbone in humans. The thymus is essential to the development of the body's system of immunity beginning in fetal life (i.e., before birth). The thymus processes white blood cells (lymphocytes; see), which kill foreign cells and stimulate other immune cells to produce antibodies (see). An important function of the thymus is to weed out lymphocytes that react to proteins produced by the body (self-antigens), thus preventing autoimmune disease. The gland grows throughout childhood until puberty and then gradually decreases in size. See Thymosin.

TISSUE: A collection of similar cells acting together to perform a particular function. There are four basic tissues in the body: epithelial, connective, muscle, and nerve.

TITER: (Also titre.) A laboratory measurement of the amount—or concentration—of a given compound in solution.

T LYMPHOCYTE PROLIFERATION ASSAY: Measures the strength of response of T memory cells (see)—a subgroup of T lymphocytes (see)—to HIV.

T LYMPHOCYTES: See T Cells.

TOXICITY: The extent, quality, or degree of being poisonous or harmful to the body.

TOXOPLASMIC ENCEPHALITIS: See Toxoplasmosis.

TOXOPLASMOSIS: Toxoplasmosis is an infection that is caused by the protozoan (see protozoa) parasite, *Toxoplasma gondii*. The parasite is carried by cats, birds, and other animals, and is found in soil contaminated by cat feces and in meat, particularly pork. The parasite can infect the lungs, retina of the eye, heart, pancreas, liver, colon, and testes. Once *T. gondii* invades the body, it remains there, but the immune system in a healthy person usually prevents the parasite from causing disease. If the immune system becomes severely damaged, as in HIV-

infected persons, or is suppressed by drugs, *T. gondii* can begin to multiply and cause severe disease. In HIV-infected persons, the most common site of toxoplasmosis is the brain. When *T. gondii* invades the brain, causing inflammation, the condition is called toxoplasmic encephalitis. While the disease in HIV-infected persons can generally be treated with some success, lifelong therapy is required to prevent its reoccurrence.

TRANSAMINASE: A liver enzyme. A laboratory test that measures transaminase levels is used to assess the health of the liver.

TRANSCRIPTION: The process of constructing a messenger RNA (see) molecule, using a DNA molecule as a template (see), with the resulting transfer of genetic information to the messenger RNA. As related to HIV: The process by which the provirus produces new viruses. RNA (see) copies, called messenger RNA, must be made that can be read by the host cell's protein-making machinery. Cellular enzymes, including RNA polymerase II, facilitate transcription. The viral genes may partly control this process. For example, *tat* (see) encodes a protein that accelerates the transcription process by binding to a section of the newly made viral RNA. See Integration; Ribonucleic Acid.

TRANSFER FACTOR: A fraction of white blood cells that apparently "transfers" capability to mount an immune response to a specific antigen (see).

TRANSFUSION: 1. The process of transfusing fluid (such as blood) into a vein. 2. The transfer of whole blood or blood products from one individual to another.

TRANSLATION: As related to HIV: The process by which HIV messenger RNA (see) is processed in a cell's nucleus (see) and transported to the cytoplasm (see), the cellular material outside the nucleus. In the cytoplasm, the cell's protein-making machinery translates the messenger RNA into viral protein and enzymes (see).

TRANSMISSION: In the context of HIV disease: HIV is spread most commonly by sexual contact with an infected partner. The virus can

enter the body through the mucosal lining of the vagina, vulva, penis, rectum, or, rarely, the mouth during sex. The likelihood of transmission is increased by factors that may damage these linings, especially other sexually transmitted diseases that cause ulcers or inflammation. HIV also is spread through contact with infected blood, most often by the sharing of drug needles or syringes contaminated with minute quantities of blood containing the virus. Children can contract HIV from their infected mothers during either pregnancy or birth, or postnatally, through breast-feeding. In developed countries, HIV is now only rarely transmitted by transfusion of blood or blood products because of screening measures.

TREATMENT IND: A program to provide experimental treatments to a class of patients who lack satisfactory alternative treatments. IND stands for Investigational New Drug (see) application, which is part of the process to get approval from the FDA for marketing a new prescription drug in the U.S.

TRIGLYCERIDE: A compound made up of a fatty acid (such as oleic, palmitic, or stearic acid) and glycerol. Triglycerides make up most animal and vegetable fats and are the basic water-insoluble substances (lipids) that appear in the blood where they circulate. In the blood they are bound to proteins, forming high- and low-density lipoproteins. Elevations of triglyceride levels (particularly in association with elevated cholesterol) have been correlated with the development of atherosclerosis, the underlying cause of some heart diseases and stroke. In relation to HIV disease, there are some patients receiving combination therapies who have experienced significant elevation in their triglyceride levels.

T SUPPRESSOR CELLS: T lymphocytes (see) responsible for turning the immune response off after an infection is cleared. They are a subset of the CD8+ lymphocytes (see).

TUBERCULIN SKIN TEST (TST): A purified protein derivative (PPD; see) of the tubercle bacilli, called tuberculin, is introduced into the skin

by scratch, puncture, or intradermal injection. If a raised, red, or hard zone forms surrounding the test site, the person is said to be sensitive to tuberculin, and the test is read as positive.

TUBERCULOSIS (TB): A bacterial infection caused by *Mycobacterium tuberculosis*. TB bacteria are spread by airborne droplets expelled from the lungs when a person with active TB coughs, sneezes, or speaks. Exposure to these droplets can lead to infection in the air sacs of the lungs. The immune defenses of healthy people usually prevent TB infection from spreading beyond a very small area of the lungs. If the body's immune system is impaired because of infection with HIV, aging, malnutrition, or other factors, the TB bacterium may begin to spread more widely in the lungs or to other tissues. TB is seen with increasing frequency among persons infected with HIV. Most cases of TB occur in the lungs (pulmonary TB). However, the disease may also occur in the larynx, lymph nodes, brain, kidneys, or bones (extrapulmonary TB). Extrapulmonary TB infections are more common among persons living with HIV. See Multidrug Resistant TB.

TUMOR NECROSIS FACTOR (TNF): A cytokine (see), produced by macrophages (see), which helps activate T cells (see). It also may stimulate HIV activity. TNF levels are very high in persons with HIV, and the molecule is suspected to play a part in HIV-related wasting, neuropathy, and dementia (see entries for these terms). TNF triggers a biochemical pathway that leads to the programmed form of cell suicide known as apoptosis (see). It also activates a key molecule that can block this very pathway, and so set up a delicate life–death balance within the cell.

V3 LOOP: Section of the gp120 (see) protein on the surface of HIV. Appears to be important in stimulating neutralizing antibodies (see).

VACCINATION: Inoculation (see) of a substance (i.e., the vaccine) into the body for the purpose of producing active immunity against a disease. See Vaccine.

VACCINE: A substance that contains antigenic components from an infectious organism. By stimulating an immune response—but not the disease—it protects against subsequent infection by that organism. There can be preventive vaccines (e.g., measles or mumps) as well as therapeutic (treatment) vaccines. See Therapeutic HIV Vaccine; Antigen.

VACCINIA: A cowpox virus, formerly used in human smallpox vaccines. Employed as a vector in HIV vaccine research to transport HIV genes into the body. See Vaccination; Vector.

VAGINAL CANDIDIASIS: Infection of the vagina caused by the yeast-like fungus *Candida* (see) (especially *Candida albicans*). Symptoms include, pain, itching, redness, and white patches in the vaginal wall. It can occur in all women, but is especially common in women with HIV infection. The usual treatment is a cream applied locally to the vagina. Women with HIV infection may experience frequent re-occurrence of symptoms and may require systemic medications in order to treat these symptoms successfully. (See also Candidiasis.)

VALLEY FEVER: See Coccidioidomycosis.

VARIABLE REGION: The part of an antibody's structure that differs from one antibody (see) to another.

VARICELLA ZOSTER VIRUS (VZV): A virus in the herpes family that causes chicken pox during childhood and may reactivate later in

life to cause herpes zoster (shingles; see) in immunosuppressed individuals.

VECTOR: A nonpathogenic bacterium or virus used to transport an antigen (see) into the body to stimulate protective immunity (e.g., in vaccine; see).

VERTICAL TRANSMISSION: Transmission (see) of a pathogen such as HIV from mother to fetus or baby during pregnancy or birth. See Perinatal Transmission.

VIDEX: See Didanosine.

VIRAL BURDEN: The amount of HIV in the circulating blood. Monitoring a person's viral burden is important because of the apparent correlation between the amount of virus in the blood and the severity of the disease: sicker patients generally have more virus than those with less advanced disease. A new, sensitive, rapid test—called the viral load assay for HIV-1 infection—can be used to monitor the HIV viral burden. This procedure may help clinicians to decide when to give anti-HIV therapy. It may also help investigators determine more quickly if experimental HIV therapies are effective. See Viral Load Test; Polymerase Chain Reaction.

VIRAL CORE: 1. Typically a virus contains an RNA (ribonucleic acid; see) or DNA (deoxyribonucleic acid) core of genetic material surrounded by a protein coat. 2. As related to HIV: Within HIV's envelope is a bullet-shaped core made of another protein, p24 (see), that surrounds the viral RNA. Each strand of HIV RNA contains the virus' nine genes. Three of these—*gag*, *pol*, and *env*—are structural genes that contain information needed to make structural proteins. The *env* gene, for example, codes for gp160 (see), a protein that is later broken down to gp120 (see) and gp41 (see). See Surrogate Marker.

VIRAL CULTURE: A laboratory method for growing viruses.

VIRAL ENVELOPE: As related to HIV: HIV is spherical in shape with a diameter of 1/10,000 of a millimeter. The outer coat, or envelope, is composed of two layers of fat-like molecules called lipids, taken from the membranes of human cells. Embedded in the envelope are numerous cellular proteins, as well as mushroom-shaped HIV proteins that protrude from the surface. Each mushroom is thought to consist of four gp41 (see) molecules embedded in the envelope. The virus uses these proteins to attach to and infect cells.

VIRAL LOAD TEST: In relation to HIV: Test that measures the quantity of HIV RNA (see) in the blood. Results are expressed as the number of copies per milliliter of blood plasma. Research indicates that viral load is a better predictor of the risk of HIV disease progression than the CD4 (see) count. The lower the viral load the longer the time to AIDS diagnosis and the longer the survival time. Viral load testing for HIV infection is being used to determine when to initiate and/or change therapy. See Viral Burden.

VIRAMUNE: See Nevirapine.

VIREMIA: The presence of virus in the bloodstream. See Sepsis.

VIRICIDE: Any agent that destroys or inactivates a virus.

VIRION: A virus particle existing freely outside a host cell. A mature virus.

VIROLOGY: The study of viruses and viral disease.

VIRUS: Organism composed mainly of nucleic acid within a protein coat, ranging in size from 100 to 2,000 angstroms (unit of length; 1 angstrom is equal to 10^{-10} meters). When viruses enter a living plant, animal, or bacterial cell, they make use of the host cell's chemical energy and protein—and nucleic acid—synthesizing ability to replicate themselves. Nucleic acids (see) in viruses are single stranded or double stranded, and may be DNA (deoxyribonucleic acid; see) or RNA

(ribonucleic acid; see). After the infected host cell makes viral components and virus particles are released, the host cell is often dissolved. Some viruses do not kill cells but transform them into a cancerous state; some cause illness and then seem to disappear, while remaining latent and later causing another, sometimes much more severe, form of disease. In humans, viruses cause—among others—measles, mumps, yellow fever, poliomyelitis, influenza, and the common cold. Some viral infections can be treated with drugs.

VISCERAL: Pertaining to the major internal organs.

WASTING SYNDROME: See AIDS Wasting Syndrome.

WESTERN BLOT: A laboratory test for specific antibodies (see) to confirm repeatedly reactive results on the HIV ELISA (see) or EIA tests. In the U.S., Western Blot is the validation test used most often for confirmation of these other tests.

WHITE BLOOD CELLS: See leukocytes.

WILD-TYPE VIRUS: The original type of HIV—unchanged by having developed any resistance to antiretroviral drugs (see). Also, 1. the prevalent type of a virus in the host population before genetic manipulation or mutation; 2. virus that is isolated from a host as opposed to one grown in a laboratory culture (see Primary Isolates).

WINDOW PERIOD: Time from infection with HIV until detectable seroconversion (see).

YEAST INFECTION: See Candidiasis.

ZALCITABINE: A nucleoside reverse transcriptase inhibitor (see) first approved by FDA in 1992 and used in combination with antiretroviral agents (see) for the treatment of HIV infection in patients 13 years of age and older. Also called ddC, HIVID.

ZERIT: See Stavudine.

ZIAGEN: See Abacavir.

ZIDOVUDINE: A nucleoside reverse transcriptase inhibitor (see) first approved by FDA in 1987 and used in combination with other antiretroviral agents (see) for the treatment of HIV infection in adults and children 3 months to 12 years of age. Also FDA approved (08/08/94) for use in HIV-infected pregnant women beginning between 14 and 34 weeks gestation and during labor, and for use in newborn babies of HIV-infected mothers. Also called AZT, ZDV, and Retrovir and available with Lamivudine as Combivir (see).

ZINC FINGERS: Chains of amino acids (see) found in cellular protein which bind to DNA (see) or messenger RNA (see), and play important roles in a cell's life cycle. They are called zinc fingers because they capture a zinc ion, which contributes to the array's binding to RNA or DNA. There are two zinc fingers in HIV's nucleocapsid (see). Zinc fingers are involved in binding and packaging viral RNA into new virions (see) budding from an infected host cell. The nucleocapsid protein and the zinc fingers also play a role during the process of reverse transcription (see Reverse Transcriptase).

ZINC FINGER INHIBITORS: A class of experimental anti-HIV drugs which prevents the nucleocapsid (see) part of the Gag protein of HIV—which contains the zinc finger amino acids (see) structures—from capturing and packaging new HIV genetic material into newly budding virions (see).

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